APHASIA AFTER STROKE: THE SPEAK STUDY

Hanane El Hachioui

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acute
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rehabilitation
reliability
screening
semantics
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syntax
validity

APHASIA AFTER STROKE: THE SPEAK STUDY

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1 GENERAL INTRODUCTION

APHASIA

Aphasia is a disorder of the production and comprehension of written and spoken language as a result of acquired brain damage. This damage is located in the dominant hemisphere, which is the left hemisphere for nearly all the right-handers and for about 70% of the left-handers.[1-2] The evolvement of aphasia is usually rapid if caused by a head injury or stroke, but can also evolve slowly as a consequence of a brain tumor, infection, or dementia. The most common cause of aphasia is a stroke.

The number of people living with aphasia in the Netherlands is approximately 30,000. Every year, about 9,600 new cases of aphasia after stroke occur.[3] The first and main question of patients and their family in the acute stage of stroke is whether the symptoms will decrease, and the patient will ever be able to speak and comprehend as before the stroke again.

The severity of aphasia after stroke ranges from having difficulties with infrequent words, complex sentences and texts, to being completely unable to speak, comprehend, read, or write. The impact on one's ability to communicate is devastating, not only for the patients with aphasia but also for their family and friends. Patients with aphasia are no longer sufficiently capable of expressing and clarifying their thoughts, wishes, and needs, which puts an aphasic patient at a higher risk for depression.[4] Ninety percent of persons with aphasia feel socially isolated.[3] Stroke patients with aphasia also have a higher mortality rate and a worse rehabilitation outcome than stroke patients without aphasia.[5]

Aphasia is traditionally classified in anatomically based categories such as Wernicke, Broca, and conduction aphasia. However, about 30% of aphasia patients do not fit into one of these traditional categories.[6] In addition, there is a huge variation in severity among patients with the same classical typology. More importantly, this traditional type of classification does not specify which of the main 3 linguistic components of communication, i.e. semantics (word meaning), phonology (word sound), and syntax (sentence structure), are affected. Disruptions of these various linguistic components are not restricted to a specific type of aphasia: lexical-semantic disorders may occur in all aphasia types, phonological disorders are mostly observed in Broca's, Wernicke's, and conduction aphasia, and syntactic disorders are particularly observed in Broca's and Wernicke's aphasia. In patients with global aphasia all linguistic components are severely affected.

Disorders of any of the linguistic components may lead to problems in word finding and sentence building, which often cause a severe handicap in daily life communication. Therefore, data on the occurrence, prognosis, and recovery of disorders of the different linguistic components in aphasia after stroke are crucial. Information on the patients' performance on these linguistic components is important in order to refine diagnosis and treatment. The available therapeutic methods are mainly directed at the various linguistic components or communicative skills and not at aphasia subtypes.[7] The effect of aphasia treatment is outside the scope of this thesis as well as some other factors that influence daily life communication in addition to the performance on the linguistic components, such as pragmatics. For example, patients with aphasia often complain about having communicative difficulties when they are at a party, even though they don't have difficulties communicating in one-to-one situations.

Aphasia is reported to be associated with impairments in other cognitive domains such as executive functioning[8] and memory[9], which are also common sequelae of stroke. Insight into non-linguistic cognitive functioning in aphasic patients is clinically very relevant, because information on cognitive performance has been reported to be a significant predictor for the outcome of linguistic treatment.[10]

OUTLINE OF THIS THESIS

In this thesis, I address the natural course and prognosis of aphasia after stroke in a large Dutch multicenter prospective study, the Sequential Prognostic Evaluation of Aphasia after stroKe study, known as the SPEAK study.

In Chapter 2, I present a systematic review on screening tests that are available for differentiating between stroke patients with and without aphasia. The risk of bias of the various identified screening tests is discussed and the test with the best evidence of reliability and accuracy is presented.

Chapter 3 explores whether investigating the recovery of the main 3 linguistic components separately is feasible by means of a pilot study.

Chapter 4 presents the psychometric properties of the ScreeLing, a screening test to detect disorders of the main 3 linguistic components, and the occurrence of these disorders in the acute stage of stroke.

Chapter 5 focuses on a prognostic study that was aimed at predicting verbal outcome of aphasia at 1 year after stroke. I investigated the prognostic value of linguistic, demographic, and clinical stroke characteristics.

Chapter 6 covers an observational 1-year follow-up study in which the recovery of semantics, phonology, and syntax was examined as well as of verbal communication and of aphasia severity.

In Chapter 7, I describe the prevalence and course of non-linguistic cognitive impairments in the first year after stroke, and their association with aphasia and functional outcome.

Chapter 8 discusses the main findings, clinical implications, and suggestions for future research. Finally, the results of the studies presented in this thesis are summarized in Chapter 9.

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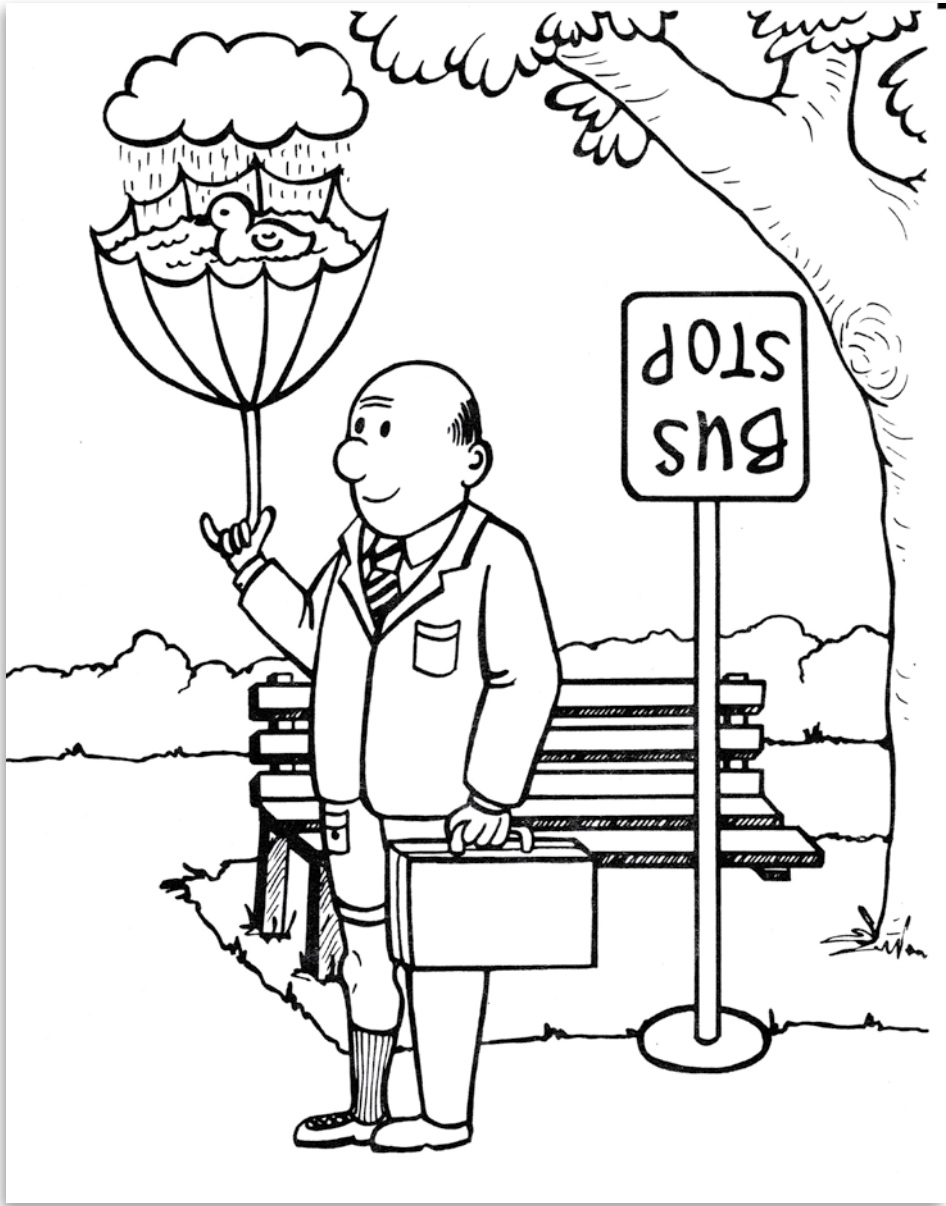
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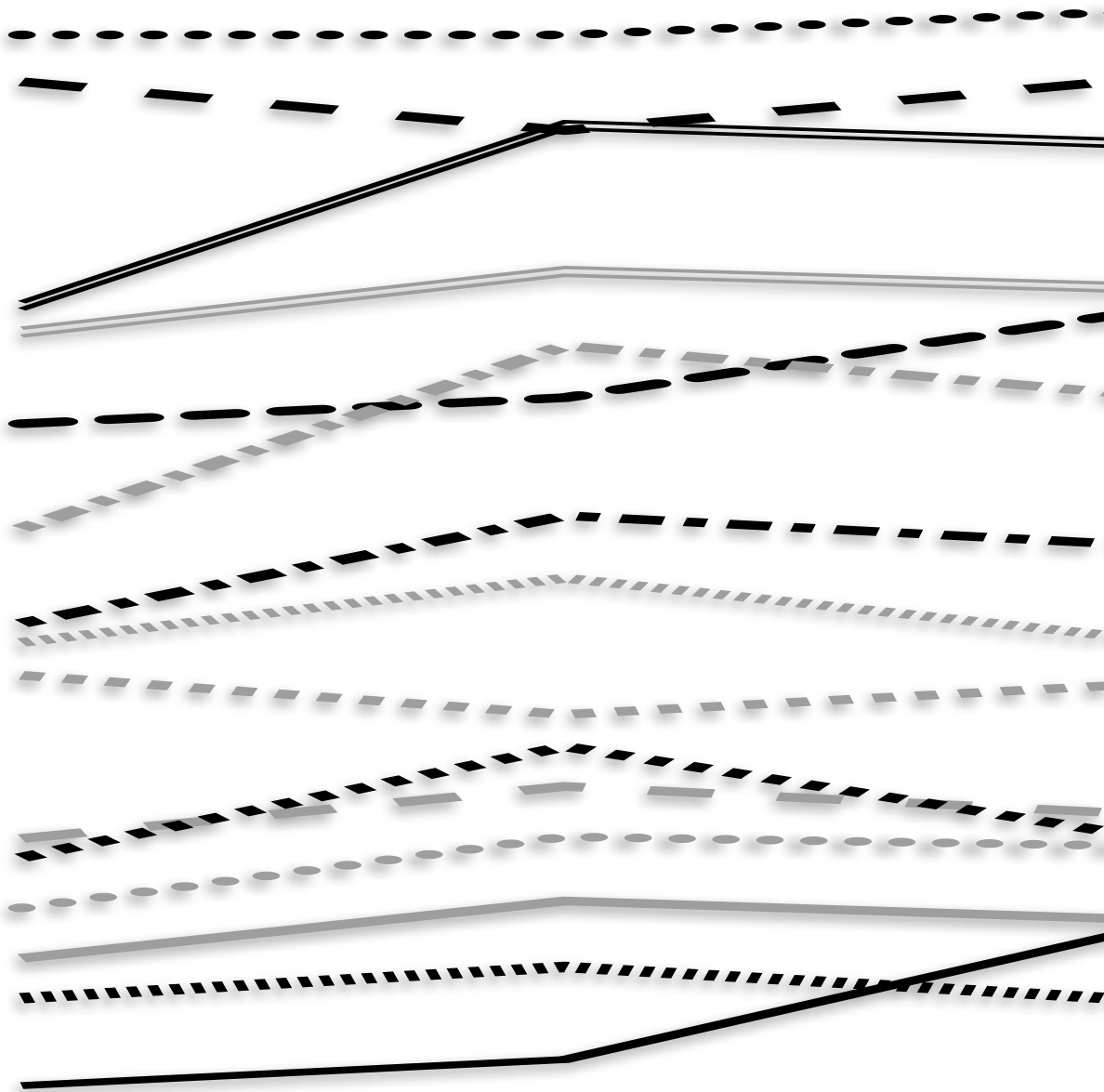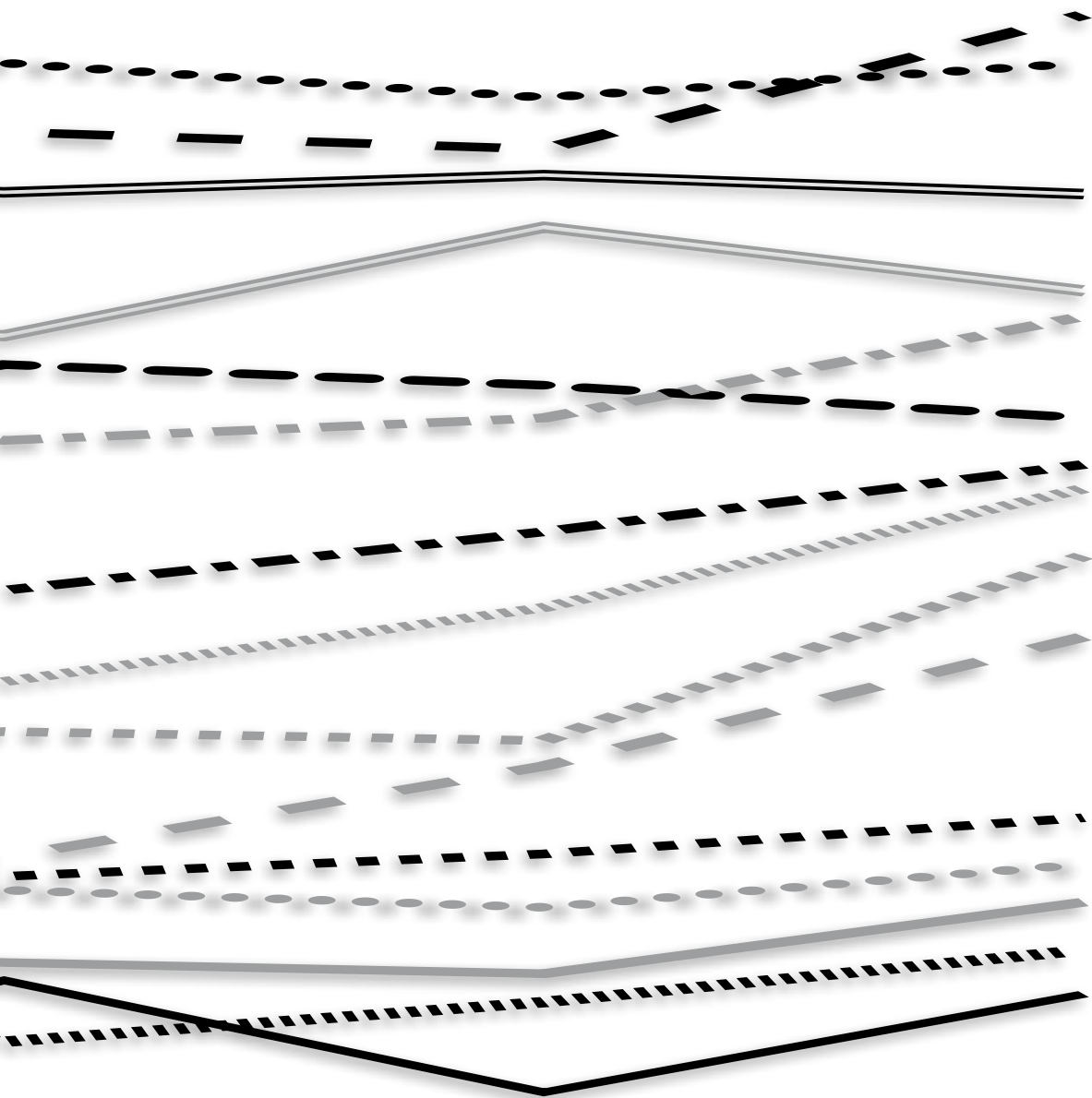
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**A 3-YEAR EVOLUTION
OF LINGUISTIC DISORDERS
IN APHASIA AFTER STROKE**

ABSTRACT

Background

Aphasia recovery after stroke has been the subject of several studies, but in none the deficits of the various linguistic components were examined, even though in the diagnosis and treatment of aphasia the emphasis lays more and more on these linguistic component disorders.

Objective

In this observational prospective follow-up study we explored whether it is meaningful to investigate the recovery of semantics, phonology, and syntax separately.

Methods

Fifteen patients with aphasia were assessed at 3 and 10 days, 7 weeks, 4 and 7 months, and 3 years after stroke. We used the ScreeLing to assess the patients' performance on the 3 linguistic components, the Aphasia Severity Rating Scale (ASRS) (verbal communication), and the Token Test.

Results

Group results showed improvement for the overall ScreeLing ($p < 0.01$) and its subparts semantics ($p < 0.01$) and syntax ($p < 0.01$) up to 7 weeks, just as for the Token Test ($p < 0.01$). Phonology improved up to 4 months ($p < 0.05$) and the ASRS up to 7 months ($p < 0.05$).

Conclusion

The recovery pattern of the 3 linguistic components did not follow a parallel course, with a great deal of variability in linguistic recovery curves between as well as within patients. These results suggest that it is meaningful to assess the recovery of the linguistic components separately, starting from the acute stage after stroke.

INTRODUCTION

The recovery of aphasia after stroke is of great clinical importance, because of its large impact on communication, both for patients and their families. Adequate communication in a social context requires intact linguistic processing on the main linguistic components, that is, semantics, phonology, and syntax.[1] These linguistic components can be affected selectively in aphasia.[2-4]

The linguistic deficits, each manifested in a different way, determine the quality of verbal communication. Restoration of communication requires the integration of the linguistic components. Therefore, it is important to get more insight into the recovery pattern of each linguistic component separately.

Although in the diagnosis and treatment of aphasia the emphasis is more and more on the linguistic component disorders rather than on the classic aphasia syndromes, recovery studies have not taken this approach so far. The tests used in these studies are either general test batteries aimed at the language modalities such as repetition, naming, reading, writing, and comprehension[5-8], or tests that assess communicative abilities[6, 8-10] (Table 1). It is generally agreed that the major part of recovery occurs within the first few months, but the exact period varies among studies. The largest recovery is reported to occur within 3 months[6, 10], within the first 4 weeks[5], or even within the first 2 weeks after stroke onset[9, 11-12]. Few studies report a longer period of recovery, that is, during the first 6 months and from 6 months to 1 year.[7-8] This variation in observations is due to the large differences in the time between onset and first assessment (admission - 2 months after onset) as well as between the final assessment (1 month - 2 years after onset), in the frequency at which the assessments took place (3 - 5 follow-up assessments), and in the time interval between the baseline and the first follow-up assessment (1 week - 4 months). Consequently, very early as well as late recovery could have been missed.

Up to now, no recovery study has investigated the evolution of the individual linguistic components, whereas selective disorders are present in about 30% of patients with aphasia and can be apparent already in the first week after stroke.[13] The aim of this pilot study was to investigate the recovery of the individual linguistic components in patients with aphasia from the acute stage up to 3 years after stroke.

METHODS

Patients

Patients were recruited from the Erasmus Stroke Study. This is a prospective registry of patients with transient ischemic attack or stroke who are referred to the Erasmus MC University Medical Center.

Adult Dutch native speakers who had a first-ever stroke with aphasia due to intracerebral hemorrhage or infarction as judged by a neurologist and clinical linguist were eligible for inclusion. Patients who could be assessed within the first 2 weeks after stroke were included. Exclusion criteria were severe visual or auditory problems, illiteracy, mental retardation, or pre-stroke dementia.

Table 1. Aphasia Recovery Studies after Stroke

Study (first author, year, ref)	Tests Used for Follow-Up	Test Characteristics	Time-Points Since Onset & Findings
Pashek, 1988[11] n aphasics = 43	1) WAB 2) Recordings of communicative behavior	1) Test for language function and aphasia type classification: verbal fluency, language information content, comprehension, repetition, and naming 2) Semi-structured conversational interactions to elicit communicative strengths/ weaknesses	0-5 days, daily during hospital stay, 1, 2, 3, 4-6, 7-12 months: most improvement at 2 weeks for all aphasia syndromes except conduction aphasia, which evolved at 6 months
Sarno, 1979[8] n aphasics = 34	1) FCP 2) subtests of NCCEA: VN, SR, WF, and TT	1) 9-point rating scale, considers 45 everyday communication behaviors, based on observations during an informal conversation 2) 20 language performance tests covering communication modalities VN: naming objects in visual confrontation SR: repeating sentences of increasing length and grammatical complexity WF: naming as many words in 1 minute beginning with a specified letter TT: 39 verbal commands of increasing complexity: manipulating 20 plastic tokens of 2 shapes, 2 sizes, 5 colors	4, 8, 12, 26, 52 weeks: fluent and non-fluent aphasics improved most between 2 and 6 months; global aphasics improved most between 6 months and 1 year
Hartman, 1981[9] n aphasics = 44	PICA	Measures communicative ability: 18 subtests comprising speaking, auditory processing, gesture, writing, reading, copying, and visual matching	1, 2, 4 weeks: most improvement first 2 weeks
Lendrem, 1985[10] n aphasics = 52	1) PICA 2) FCP 3) SQ	1) Measures communicative ability: 18 subtests comprising speaking, auditory processing, gesture, writing, reading, copying, and visual matching 2) 9-point rating scale, considers 45 everyday communication behaviors, based on observations during an informal conversation 3) Measures functional speech	4, 10, 22, 34 weeks: most improvement between 4 and 10 weeks
Pedersen, 1995[12] n aphasics = 330	SSS, aphasia scale	Aphasia scale divides aphasia into severe, moderate, mild, and no aphasia	At admission, weekly during hospital stay, 6 months: 95% of mild aphasics improved most in the first 2, moderate aphasics in 6, and severe aphasics in 10 weeks

Table 1. Aphasia Recovery Studies after Stroke – *continued*

Study (first author, year, ref)	Tests Used for Follow-Up	Test Characteristics	Time-Points Since Onset & Findings
Nicholas, 1993[7] n aphasics = 24	BASA	61-items, to identify and quantify preserved communicative abilities in severely aphasics: auditory and reading comprehension, praxis, gesture recognition, visuo-spatial tasks, oral-gestural expression, and signature	1-2, 6, 12, 18, 24 months: greatest improvement first 6 months; next greatest improvement between 6 and 12 months
Laska, 2001[6] n aphasics = 119	1) Reinvang's 'Grunntest for afasi' 2) ANELT	1) Similar to WAB: measures fluency, naming, comprehension, repetition, writing, reading 2) A functional 10-item test of familiar daily life scenarios: the understandability of the patient's message and the intelligibility of the utterance are each rated on a 5-point scale	11 days, 3, 6, 18 months: most improvement, first 3 months
Bakheit, 2007[5] n aphasics = 62	WAB	Test for language function and aphasia type classification: verbal fluency, language information content, comprehension, repetition, and naming	At baseline, 4, 8, 12, 24 weeks: largest improvement for all aphasia types first 4 weeks; progressively smaller improvement in subsequent weeks with Broca's aphasia showing the best rate and extent of recovery, and anomic and conduction aphasia relatively the worst

ref, reference; ANELT, Amsterdam-Nijmegen-Everyday-Language-Test; BASA, Boston Assessment of Severe Aphasia; FCP, Functional Communication Profile; NCCEA, Neurosensory Center Comprehensive Examination for Aphasia; PICA, Porch Index of Communicative Ability; SR, sentence repetition; SSS, Scandinavian Stroke Scale; SQ, Speech Questionnaire; TT, Token Test; VN, visual naming; WAB, Western Aphasia Battery; WF, word fluency.

Six follow-up assessments took place: at 2-4 (T1), 9-12 days (T2), 5-7 (T3), 10-15 (T4), 23-28 weeks (T5), and at 3 years after stroke (T6). The patients were included while admitted to hospital and followed in the successive settings, that is, nursing homes, rehabilitation centers, or at the patients' homes.

Informed written consent was obtained from the patients or their close relatives before their inclusion in the study. At 3 years after stroke all patients were first contacted in writing referring to the earlier assessments. When verbal consent was given, an appointment was made. This study was approved by the local medical ethics committee.

Assessments

1. The ScreeLing assesses 3 linguistic components (i.e. semantics, phonology, syntax) and was specifically developed for use in acute stroke patients with aphasia. The overall accuracy of the research version of the ScreeLing for detecting aphasia is 92% with a sensitivity of 86% and a specificity of 96%.[13] These were determined by comparing the ScreeLing overall-score with a combined reference diagnosis. Patients were labeled with the reference diagnosis of 'aphasia' if they had aphasia according to at least 2 of the following measures: (*i*) the Token Test[14], (*ii*) the independent judgment of a neurologist, (*iii*) the independent judgment of a linguist. The ScreeLing comprises 72 items. Each linguistic component is tested with 24 items, divided over 4 tasks. Semantics consists of word-picture matching, identifying semantically anomalous sentences, verbal semantic association, and odd-word-out. Phonology consists of word repetition, reading aloud, word reversal, and auditory lexical decision. Syntax consists of sentence-picture matching, judgment syntactic correctness, selecting the correct sentence, and repetition of sentences consisting of mainly function words.[13]
2. Spontaneous speech, a way to measure verbal communication, was elicited in a 10-minute semi-standardized interview according to the Aachen Aphasia Test-procedure[15], and evaluated according to the Aphasia Severity Rating Scale of the Boston Diagnostic Aphasia Examination[16]. This is a 6-point scale varying from 0 'no usable speech or auditory comprehension' to 5 'minimal discernible speech handicap' (see appendix II).
3. The Token Test measures the presence and the severity of aphasia.[14] This version consists of 36 items with a cut-off score of 29.

Statistical Analyses

Because of the sample size nonparametric tests were used to analyze the data. Friedman tests were first conducted to establish whether there was a difference in scores over the 6 assessments. In case of statistical significance, Wilcoxon Signed Ranks Tests were performed to determine which time intervals showed significant change. We used the interpolation method in case of missing data. All analyses were carried out with SPSS version 15.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

During a period of 15 months, 55 stroke patients with aphasia were included in the Erasmus Stroke Study. Fifteen of these patients met the inclusion criteria and could be assessed within the first 2 weeks after stroke. The study population consisted of 6 women and 9 men. The mean age was 67 years (standard deviation (SD) 13), ranging between 41 and 83 years. The mean length of education was 9.54 years (SD 2.47), ranging between 6 and 14 years. Nine patients were right-handed, 3 were left-handed, and of 3 patients their handedness was unknown. Fourteen patients had a stroke in the left hemisphere and 1 in the right hemisphere. Twelve patients had aphasia due to an infarction and 3 patients due to intracerebral hemorrhage. Two patients died in the first 3 weeks during follow-up and 1 patient died after 6 months. At the final assessment 12 patients could be evaluated.

If a patient's performance reached a normal range on a measure, then this measure was not used again in subsequent assessments with the exception of the final one. This was the case in 2.6% of the spontaneous speech assessments, in 19.2% of the Token Test assessments, and in 12.8% of the ScreeLing assessments. At 3 years the complete set of tests was administered in all patients. Three patients could not be assessed at 1 of the 6 time points because of illness. The data were completed using interpolation.

Mean days after stroke at each of the 6 time points are displayed in Table 2.

Table 2. Time of Assessment after Stroke in Days

T1 (SD)	T2 (SD)	T3 (SD)	T4 (SD)	T5 (SD)	T6 (SD)
3 (0.83)	10 (1.08)	51 (9.89)	101 (10.14)	193 (12.90)	1116 (112.95)

SD, standard deviation.

Recovery Pattern, Group Results

The comparison of the 6 assessments with the use of Friedman tests revealed an overall significant effect in scores on each test and subtest: ScreeLing ($\chi^2 = 7.95$, df = 5, p < 0.001), Semantics ($\chi^2 = 32.35$, df = 5, p < 0.001), Phonology ($\chi^2 = 26.44$, df = 5, p < 0.001), Syntax ($\chi^2 = 40.42$, df = 5, p < 0.001), Aphasia Severity Rating Scale ($\chi^2 = 40.53$, df = 5, p < 0.001), and Token Test ($\chi^2 = 32.39$, df = 5, p < 0.001). The scores of each measure are displayed in Table 3.

Table 3. Scores of Each Assessment during Follow-Up

	T1 (3 days)	T2 (10 days)	T3 (7 weeks)	T4 (4 months)	T5 (7 months)	T6 (3 years)
Aphasia Severity Rating Scale (maximum 5)[a]	2 (0-3)	2 (1-4)	3 (2-4)*	4 (3-4)*	4 (3-5)*	4 (3-5)
Token Test (maximum 36)[b]	11.89 (11.24)	15.81 (11.65)*	22.42 (11.56)**	23.19 (10.52)	23.73 (10.23)	23.17 (9.62)
ScreeLing total (maximum 72)[b]	34.31 (26.73)	43.15 (23.51)**	57.85 (13.13)**	59.31 (12.54)	59.92 (11.42)	59.58 (12.20)
Semantics (maximum 24)	11.38 (9.37)	14.08 (7.98)	20.08 (4.94)**	20.62 (4.35)	20.85 (4.26)	21.33 (4.52)
Phonology (maximum 24)	12.46 (9.79)	15.54 (8.92)*	18.62 (5.81)	19.77 (5.36)*	19.46 (5.13)	19.00 (5.53)
Syntax (maximum 24)	10.46 (7.94)	13.54 (7.48)**	19.15 (3.53)**	18.92 (4.61)	19.62 (4.39)	19.25 (4.25)

[a] median (interquartile range).
[b] mean (standard deviation).
*Significant improvement in relation to the preceding assessment p < 0.05; **p < 0.01 (Wilcoxon Signed Ranks test).

Changes in total ScreeLing scores revealed significant improvement between T1 and T2 (mean difference = 8.84, p = 0.008), and between T2 and T3 (mean difference = 14.7, p = 0.002). The analyses for the linguistic components showed a significant improvement from T2 to T3 in semantics (mean difference = 6, p = 0.003), from T1 to T2 and from T3 to T4 in phonology (mean difference = 3.08, p = 0.015; mean difference = 1.15, p = 0.017, respectively), and in syntax from T1 to T2 (mean difference = 3.08, p = 0.007) and from T2 to T3 (mean difference = 5.61, p = 0.002). Furthermore, there was a trend in the improvement of phonology between T2 and T3 (mean difference = 3.08, p = 0.065).

The Aphasia Severity Rating Scale showed significant improvement between T2 and T3, between T3 and T4, and between T4 and T5.

The Token Test scores increased significantly from T1 to T2 (mean difference = 3.92, p = 0.015) and from T2 to T3 (mean difference = 6.61, p = 0.005).

Thus, the overall ScreeLing as well as its semantic and syntactic components showed the same recovery pattern as the Token Test, that is, significant recovery occurring during the first 7 weeks. Phonology showed a recovery pattern more in line with the Aphasia Severity Rating Scale, that is, significant improvements further in time, up to 4 months and 7 months, respectively.

Individual Linguistic Recovery Patterns

Individual scores of the linguistic components show variability in recovery between as well as within patients. Several patients show a rather distinct linguistic recovery pattern in which the recovery of 1 component can be in accordance with the group results while the others may not. Additionally, the recovery patterns of the linguistic components are not consistent between patients. To illustrate the diversity of the recovery of the 3 linguistic components, 3 cases are presented in Figure 1.

Patient 9's semantic recovery curve appears to differ from phonology and syntax: a late versus an early recovery. The largest improvement in the semantics score was observed between 7 months and 3 years. Apparently, phonology and syntax improved mostly between the second and seventh week. The late semantic recovery of this patient contrasts with the overall group results where we found no significant increase in the linguistic component scores after 4 months. Even though this patient had a deficit in all components at baseline with the most severe deficit in semantics, at 3 years there was complete recovery with the exception of the phonological disorder.

Patient 15 had a steep increase in scores up to 7 weeks on all 3 components, which is in line with the overall group results. After 7 weeks there was little change in scores on the semantic and phonological component, but a temporary decrease occurred in the syntactic component between 7 weeks and 7 months. This patient had a severe disorder in all 3 linguistic components at baseline and improved completely at 3 years, even though there was a temporary deterioration in the syntactic component.

Finally, patient 5 seemingly had fluctuating semantic and syntactic curves with increasing as well as decreasing scores up to 7 months after onset, whereas phonology showed a steadier curve. This patient seemed to deteriorate after 7 months on all 3 components. There was no difference comparing baseline and final scores. The cause for the fluctuations and deterioration is unknown. There might have been coexisting non-linguistic cognitive deficits.

Patient 9

Patient 15

Patient 5

Time of Assessment after Stroke Onset

| ——— Semantics | ----- Phonology | ——— Syntax |

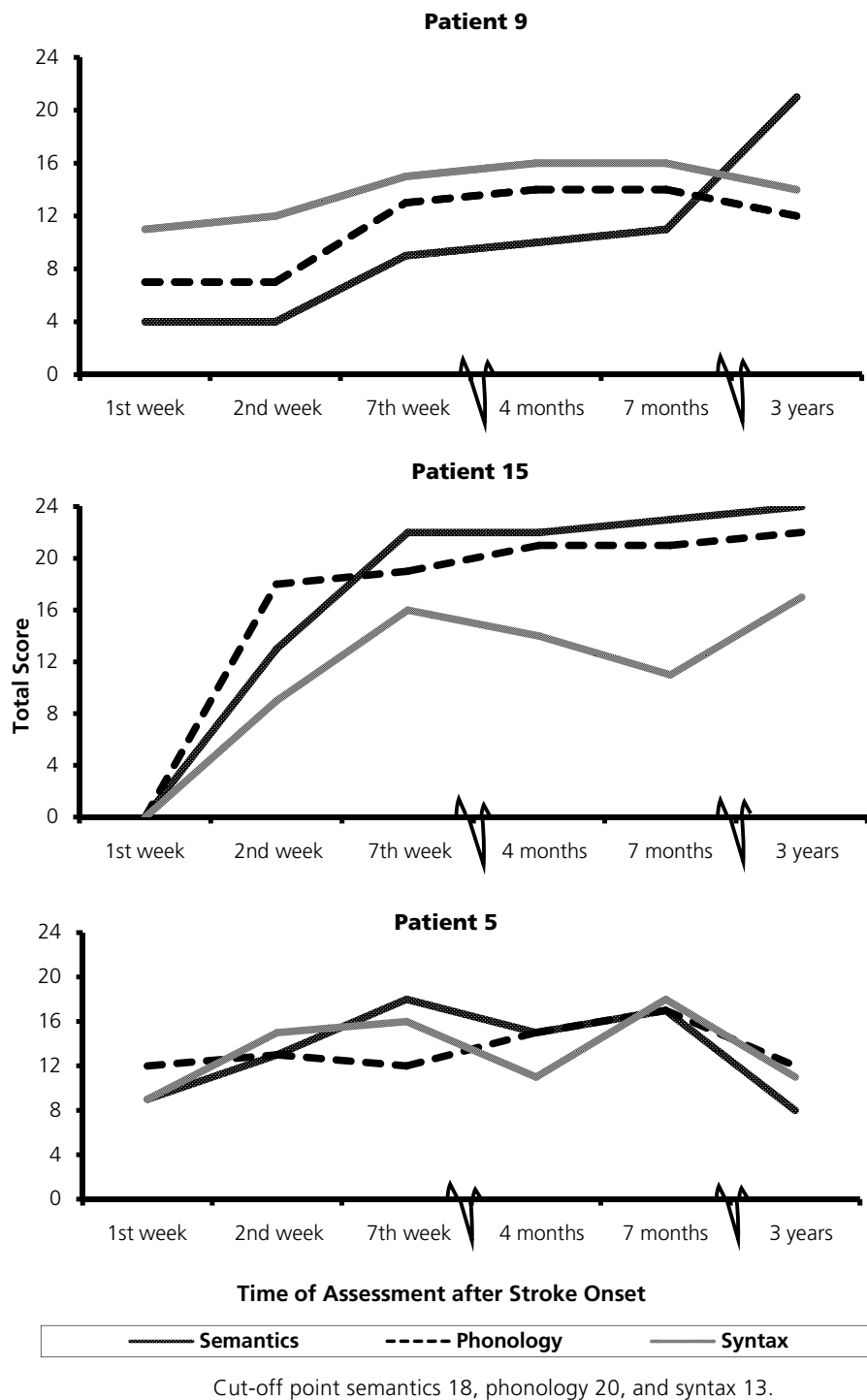Cut-off point semantics 18, phonology 20, and syntax 13.

Figure 1. Linguistic Recovery Curves of 3 Cases

These individual cases illustrate that the recovery curves of the linguistic components may show different patterns in individual patients, which is not necessarily in accordance with the group results.

DISCUSSION

The results of our pilot study indicate that it is meaningful and feasible to assess the recovery pattern of the various linguistic components, that is, semantics, phonology, and syntax in patients with aphasia after stroke. The largest improvement might occur earlier than the generally assumed period of 3 months. The scores on the Token Test, the overall ScreeLing score, and the semantics and syntax scores, each seemed to reach a plateau at 7 weeks after stroke onset, which is in line with previous recovery studies that also assessed patients early after stroke[5, 9, 11-12]. Aphasia recovery studies should be based on frequent observations in the acute stage, as this period appears to be the most susceptible for improvement.

Our group results suggest that the different linguistic components might not recover simultaneously, which illustrates the relevance of examining the linguistic components separately during course. Improvement in semantics only occurred between 10 days and 7 weeks after stroke. Improvement in phonology was not observed in this period but earlier, that is in the first 10 days and it continued between 7 weeks and 4 months after stroke. Improvement in syntax also started in the first 10 days, but ended early in contrast with phonology; syntactic improvement occurred only up to 7 weeks after stroke onset. Phonology took longer to improve even though the recovery process started as early as syntax. This difference could be due to the fact that phonology, as tested with the ScreeLing, is the only component that incorporates language production. It might be that language production takes more time to recover than receptive language modalities.[17] This appears to be supported by our results of the Aphasia Severity Rating Scale, which measures the severity of aphasia by evaluating the language expression, showing significant improvement up to 7 months after stroke. The longer-lasting recovery period of verbal communication might be related to the fact that verbal communication requires integration of the semantic, phonological, syntactic, and pragmatic abilities.

The strengths of our study are that patients were observed during a relatively long period and that we have investigated the evolution on various linguistic components in detail. The most important weaknesses of our study are the small sample size and the fact that we did not monitor therapy. For 11 patients it was documented that they received some form of aphasia therapy, for the other patients there is no information available. Even though strong evidence for the efficacy of aphasia therapy is yet to come[18-19], it is possible that the duration, frequency, and type of therapy has influenced the recovery patterns. Furthermore, the ScreeLing is not a widely available measure yet. However, the test comprises the most well-established tasks to measure semantics, phonology, and syntax.[13] The psychometric properties are currently being described in detail. Finally, we did not examine non-linguistic deficits that may influence recovery and functional outcome.[20-21]

In conclusion, this study indicates that it may be important for the assessment of aphasia after stroke to test the 3 linguistic components separately instead of using

only overall aphasia assessments. Despite its small sample size our study suggests that the recovery patterns show different dynamics on the 3 linguistic components. Furthermore, our results highlight the additional value of analyzing the results of individual patients in addition to group analyses. Patients may show highly varying patterns on each linguistic component and a distinct recovery pattern that may not comply with the generally held perceptions of aphasia recovery. On the basis of this pilot study we have decided to embark on a large multicenter study to investigate the prognosis of aphasia after stroke, the 'Sequential Prognostic Evaluation of Aphasia after stroKe (SPEAK)' study. The aim of this study, that has started in 2007 and currently involves over 140 patients, is to gain more insight into the recovery pattern of the 3 linguistic components and the predictors of the final language function. The recovery will be analyzed against the background of co-existing cognitive disorders as the presence of cognitive disorders is reported to interfere with functional outcome. Furthermore, the influence of linguistic deficits on the quality of life will be investigated.

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THE SCREELING: OCCURRENCE OF LINGUISTIC DEFICITS IN ACUTE APHASIA POST-STROKE

ABSTRACT

Background

The occurrence and nature of linguistic deficits in acute aphasia post-stroke is largely unknown, which limits the rehabilitation planning and treatment possibilities.

Objective

To investigate the occurrence of semantic, phonological, and syntactic deficits in acute aphasia with the ScreeLing after the establishment of its psychometric properties. To examine the relationship between these deficits and: (*i*) overall aphasia severity; and (*ii*) the quality of verbal communication.

Methods

The reliability and validity of the ScreeLing was established by investigating 141 patients with acute aphasia (2 weeks after stroke), 23 with chronic aphasia, and 138 healthy controls. In addition, the acute patients were assessed with the Token Test, a measure of aphasia severity, and the Aphasia Severity Rating Scale (ASRS), a measure of verbal communication.

Results

The ScreeLing was found to be valid and reliable for assessing the presence and severity of aphasia and linguistic deficits at 12 days after stroke. In 22.4% of the patients deficits were found in only 1 of the 3 linguistic components; phonology was most frequently disturbed (16.3%), compared with semantics (2.7%), and syntax (3.4%). The number of impaired linguistic components was related to aphasia severity: patients with a 3-level disorder had the lowest Token Test scores; patients with a selective phonological disorder had the highest ASRS ratings. Phonology alone explained 54.6% of the variance in the ASRS rating.

Conclusion

In the acute stage, linguistic-level deficits are already present independently of each other, with phonology affected most frequently.

INTRODUCTION

The prognosis of aphasia after stroke depends largely on its initial severity[1-3], but other factors may also play an important role[2, 4]. Regression models have so far explained only part of the variance of the outcome of aphasia[2, 5] indicating that other prognostic factors have not yet been discovered. For example, the nature of the linguistic disorder may be an important prognostic factor for aphasia outcome.

The only data available are about the frequencies of aphasia subtypes in acute stroke, and these are inconsistent. For instance, the reported incidence of Broca's aphasia varies from 11% to 22%[5-7], probably due to the fact that classification of aphasia is difficult in the acute stage. Many patients are not classifiable according to classic aphasia syndromes[6] and during the first weeks after stroke these syndromes tend to change.

It has been reported that domain-specific cognitive functions are good predictors for long-term cognitive outcome.[8] In addition, the prevalence of domain-specific cognitive deficits in the acute stage after stroke has been established.[9] For aphasia, this information is unknown. In order to explore whether the core linguistic components of language production and comprehension, i.e. semantics, phonology, and syntax, are relevant prognostic factors, detailed information is first needed on the nature and occurrence of the linguistic-level deficits. This information is lacking in the acute stage because of the lack of tests providing a specific linguistic-level diagnosis suitable for administration in the early stages after stroke when time-consuming tests are too much of a burden. The existing screening tools for acute aphasia usually reflect the approach taken in traditional aphasia test batteries that assess language modalities such as comprehension and reading[10-11], and are not aimed at the linguistic-level deficits.

To the best of our knowledge, the only linguistic screening test designed to assess the presence of aphasia and to differentiate linguistic-level disorders in the acute stage is the ScreeLing. In a small group study (n = 17) 30% of the patients showed selective linguistic disorders on a research version of this test.[12] The test has been refined; less accurate subtests have been replaced and, based on item analysis, further adjustments have been made in order to enhance its clinical value (see appendix III for further details).[13]

Information on the occurrence of linguistic-level disorders may be important for several reasons. Establishing the occurrence of linguistic deficits in the acute stage will provide more insight into early recovery patterns. Discovering which linguistic deficits are persistent and which may recover spontaneously provides a basis for the selection of additional, more comprehensive assessment, which may result in a better guidance during the treatment course. Furthermore, insight into the occurrence of linguistic-level deficits in the acute stage may be used to examine the impact of early linguistic profiles on final outcome.

The aims of this study were: (*i*) to report on the psychometric properties of the revised ScreeLing; (*ii*) to investigate the occurrence of linguistic-level deficits in a large group of patients with aphasia at 2 weeks after stroke; and (*iii*) to determine the relationship between linguistic-level deficits and overall aphasia severity, as well as verbal communication.

METHODS

Participants

Acute Aphasia Patients

Patients were recruited from the stroke units of 17 hospitals in the Netherlands, and screened by the local neurologist (based on clinical examination) and speech-language therapist (SLT) (based on an interview). Inclusion criteria were adult Dutch native/near-native speaker (i.e. education in Dutch started from early childhood and primary use of the Dutch language in everyday life), aphasia after a first-ever intracerebral hemorrhage or infarction, and testable with the ScreeLing[13] between 2 days and 2 weeks after stroke (i.e. alert during the administration of the test and not too ill to tolerate at least 15 minutes of the ScreeLing assessment; it was also allowed to administer the 3 linguistic components in a maximum of 3 test sessions if completed within 2 consecutive days). Exclusion criteria were pre-stroke dementia (suspected or confirmed), severe dysarthria, developmental dyslexia, severe impairment of vision and hearing (based on the medical history and standard clinical examination by the attending physician), illiteracy, and psychiatric disorder.

Chronic Aphasia Patients

Adult Dutch native/near-native speakers (i.e. education in Dutch started from early childhood and primary use of the Dutch language in everyday life) with aphasia after intracerebral hemorrhage or infarction of at least 6 months who were testable with the ScreeLing[13], were recruited from 10 treatment centers by their SLT. Exclusion criteria were dementia (suspected or confirmed), severe dysarthria, developmental dyslexia, severe impairment of vision and hearing (based on the medical history and standard clinical examination by the attending physician), illiteracy, and psychiatric disorder.

Healthy Control Group

Native/near-native speakers of Dutch (i.e. education in Dutch started from early childhood and primary use of the Dutch language in everyday life) older than 18 years were recruited by speech-language therapy Masters students from their family and friends. Exclusion criteria were cerebral disease, dementia (suspected or confirmed), developmental dyslexia, severe impairment of vision and hearing (based on an interview), illiteracy, and psychiatric disorder.

This study was approved by the central medical ethics committee of Erasmus MC University Medical Center and by the local ethical committees of the participating centers. Informed written consent was obtained from the participants and/or their close relatives prior to their inclusion in the study.

Assessments

1. The ScreeLing investigates 3 linguistic components (i.e. semantics, phonology, syntax) with a maximum score for each component of 24, and a maximum overall score of 72. Semantic tasks include word-picture matching, identifying semantically anomalous sentences, verbal semantic association, and odd-word

out; phonology comprises tasks for repetition, reading aloud, judging same/ different spoken word pairs, and matching first phoneme of a spoken word with the grapheme; syntax comprises sentence-picture matching, wh-questions, identifying syntactic incorrect sentences, and sentence completion (see appendix III).[13]

2. Spontaneous Speech, as a measure of verbal communication, was elicited in a 10-minute semi-standardized interview according to the Aachen Aphasia Test procedure[14] with 4 topics: the beginning and course of the disease; occupation; family and housing conditions; and hobbies. This interview was evaluated with the Aphasia Severity Rating Scale (ASRS) of the Boston Diagnostic Aphasia Examination[15]; a 6-point scale varying from 0 'no usable speech or auditory comprehension' to 5 'minimal discernible speech handicap' (see appendix II).

3. The Token Test (36 items) is a well-known and well-validated test to measure the presence and the severity of aphasia.[16]

For the acute patients, the assessment comprised the complete set of tests. The healthy control group was assessed with the ScreeLing and the Token Test; the chronic patients were tested twice with the ScreeLing with an interval of minimally 1 and maximally 2 weeks to investigate the test re-test reliability.

Statistical Analyses

First, we established the psychometric properties of the ScreeLing by conducting reliability and validity analyses. We calculated the internal consistency with Cronbach's α in the acute patients and healthy controls combined. The test-retest reliability was determined in the chronic patient group using Bland-Altman plots. For the construct validity, we compared the ScreeLing performance of the acute patients with that of the healthy controls with independent samples t-tests. The diagnostic accuracy of the ScreeLing and each of its 3 linguistic components was determined by means of Receiver Operating Characteristic (ROC) analysis. The sensitivity and specificity were set at the optimal cut-off point. In order to provide information on concurrent validity, correlation analyses were conducted between the ScreeLing and the Token Test, and between the ScreeLing and the ASRS.

Second, differences in mean scores between the 3 linguistic components were examined separately for the acute patients and healthy controls with paired samples t-tests in order to establish whether the subtests were equally complex for healthy speakers, and to investigate whether the linguistic components were equally impaired in aphasia. To obtain the occurrence of the linguistic-level disorders in the acute patients frequency analyses were used. For establishing possible differences in aphasia severity between subgroups of the acute patients (i.e. with a selective linguistic-level disorder, a combined disorder, or a 3-level disorder), we performed one-way ANOVA analysis and Kruskal-Wallis analysis. To identify pairwise differences we conducted post-hoc multiple comparisons tests with Bonferroni correction and Mann-Whitney tests. Finally, to determine the impact of the linguistic-level disorders in the acute patients on the ASRS, we used ordinal regression analysis.

All analyses were carried out with SPSS 15.0 (SPSS Inc., Chicago, USA).

RESULTS

Between June 2007 and June 2009, 147 acute stroke patients with aphasia were included. The complete assessment was administered at 12 days (standard deviation (SD) 2.10 days) after stroke. We excluded 6 patients whose assessments could not be completed within the time limits because no SLT was available for testing. An additional 23 chronic patients (mean time after stroke 50 months, SD 95.62 months) were included between November 2009 and December 2009. We included 138 healthy controls from April 2007 to May 2007. The participants' characteristics are shown in Table 1.

Table 1. Baseline Characteristics of the Included Participants

	Acute Patients (n=141)	Healthy Controls (n=138)	Chronic Patients (n=23)
Age, years, mean (SD) [range]	66.61 (14.90) [19-96]	55.74 (20.83) [18-88]	67.96 (14.76) [29-89]
Sex, *n (%)*			
Female	75 (53.2)	73 (52.9)	10 (43.5)
Male	66 (46.8)	65 (47.1)	13 (56.5)
Handedness (EHI), *n (%)*			
Right-handed	123 (87.2)	120 (87.0)	21 (91.3)
Left-handed	15 (10.7)	11 (8.0)	2 (8.7)
Ambidextrous	2 (1.4)	7 (5.1)	0 (0.0)
Unknown	1 (0.7)	0 (0.0)	0 (0.0)
Level of education, *n (%)*			
Unfinished elementary school	3 (2.1)	0 (0.0)	0 (0.0)
Elementary school	20 (14.2)	11 (8.0)	3 (13)
(Unfinished) Middle School	5 (3.6)	12 (8.7)	0 (0.0)
Sophomore high school or lower vocational education	44 (29.1)	15 (10.9)	9 (39.1)
Junior high school or middle vocational education	38 (27.0)	46 (33.3)	9 (39.1)
Senior high school or higher vocational education	26 (18.4)	31 (22.4)	1 (4.4)
University	5 (3.5)	23 (16.7)	0 (0.0)
Unknown	3 (2.1)	0 (0.0)	1 (4.4)
Type of stroke, *n (%)*		—	
Infarction	121 (85.8)		20 (87)
Hemorrhage	20 (14.2)		2 (8.7)
Both (infarction and hemorrhage)	0 (0.0)		1 (4.3)
Clinical localization of stroke, *n (%)*		—	
Left hemisphere	139 (98.6)		22 (95.7)
Right hemisphere	2 (1.4)		1 (4.3)

SD, standard deviation; EHI, Edinburgh Handedness Inventory.

The 3 groups were compared with Mann-Whitney tests. The acute and chronic patients did not differ significantly for age or education level. The healthy controls were younger than the acute patients ($Z = -4.46$, $p < 0.001$) and the chronic patients ($Z = -2.64$, $p = 0.008$). Their education level was higher than of the acute patients ($Z = -3.51$, $p < 0.001$) and the chronic patients ($Z = -2.95$, $p = 0.003$).

Psychometric Properties of the ScreeLing

The Cronbach's α of the total ScreeLing and phonology was 0.95; of semantics and syntax was 0.93. These results show high internal consistency for the total ScreeLing and for its linguistic components.

Test-retest reliability of the ScreeLing was examined in the chronic group. Each patient was assessed at a mean interval of 10 days (SD 3.16). The Bland-Altman plots illustrate high agreement between the 2 assessments, indicating a high stability of the ScreeLing over time (Figure 1).
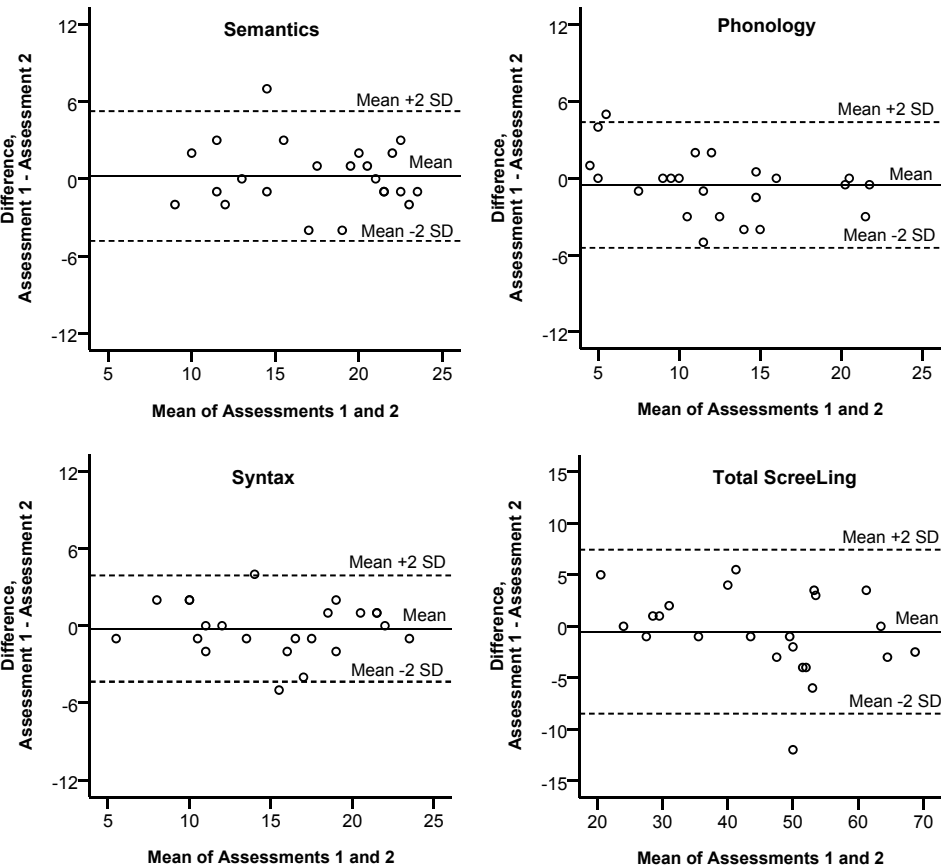

Figure 1. Bland-Altman Plots (n = 23)

The comparison of the performances on the ScreeLing of the acute patients and the healthy controls revealed an overall significant difference on the total ScreeLing and its linguistic components (Table 2).

Table 2. Construct Validity: Mean Total ScreeLing and Linguistic Component Scores for the Acute Patients and Healthy Controls

	Acute patients (n=141) Mean (SD) [SE]	Healthy controls (n=138) Mean (SD) [SE]	Mean Difference (95% CI)	p (independent samples t-tests)
Semantics	19.22 (5.60) [0.47]	23.63 (0.63) [0.05]	4.41 (3.47-5.35)	<0.001
Phonology	16.98 (6.06) [0.51]	23.69 (0.63) [0.05]	6.71 (5.70-7.73)	<0.001
Syntax	17.96 (5.76) [0.49]	23.53 (0.77) [0.07]	5.57 (4.60-6.54)	<0.001
Total ScreeLing	54.16 (16.14) [1.36]	70.85 (1.38) [0.12]	16.70 (14.0-19.39)	<0.001

SD, standard deviation; SE, standard error; CI, confidence interval.

An ROC analysis showed that the ScreeLing discriminates accurately (0.94) between aphasic patients and healthy controls (Table 3). The optimal cut-off score for the total ScreeLing was 68, i.e. patients scoring less than 68 were classified as aphasic. This led to a sensitivity of 0.94 and a specificity of 0.81 with an overall correct classification of 0.88.

Table 3. ScreeLing and its Linguistic Components: Accuracy, Sensitivity, and Specificity (n = 279)

	Accuracy	Optimal cut-off point	Sensitivity	Specificity
Semantics	0.79	22	0.94	0.56
Phonology	0.94	22	0.93	0.83
Syntax	0.87	22	0.91	0.74
Total ScreeLing	0.94	68	0.94	0.81

The ScreeLing and its linguistic components correlated significantly with the Token Test and the ASRS in the acute aphasic patients (Table 4). The Token Test showed the strongest correlation with the overall ScreeLing score. The ASRS was most related to phonology as this is the only part of the ScreeLing that incorporates language production. The high similarity and the significant relationships between the ScreeLing and the other 2 aphasia tests suggested a good concurrent validity.

Table 4. Concurrent Validity: Comparing ScreeLing with Token Test and ASRS (n = 141)

	Token Test (Pearson)	ASRS (Spearman's)	p
Semantics	0.79	0.58	<0.001
Phonology	0.80	0.73	<0.001
Syntax	0.85	0.67	<0.001
Total ScreeLing	0.88	0.73	<0.001

ASRS, Aphasia Severity Rating Scale.

Selective Linguistic Disorders

We examined possible differences in mean scores between the 3 linguistic components with paired samples t-tests (Table 2). In the healthy control group there was a significant difference between phonology and syntax (p = 0.038, 95% confidence interval (CI) = 0.0 to 0.32), in favor of phonology. In the acute group there was a significant difference between all 3 components, i.e. between semantics and phonology (p < 0.001, 95% CI = 1.49 to 2.99), between semantics and syntax (p < 0.001, 95% CI = 0.71 to 1.81), and between phonology and syntax (p = 0.001, 95% CI = -1.56 to -0.40). The phonological component showed the lowest scores; semantics scored the highest.

To ascertain the occurrence of linguistic-level deficits in the first 2 weeks after stroke, we conducted frequency analyses (Table 5). Selective linguistic-level disorders occurred in 22.4% of the patients; they scored lower than 22 on 1 particular component, whereas their score on the other 2 linguistic components was normal, i.e. >22. A selective phonological disorder occurred most frequently (16.3%). These patients had a mean phonology score of 19.71 (SD 1.99), a mean Token Test score of 27.20 (SD 5.41), and 79.2% of them had a high ASRS rating (score 4 or 5). Among the combined disorders of 2 linguistic components, the most frequent was the combination of a phonological and syntactic deficit (13.6%). Patients with this combination had a mean phonology score of 17.60 (SD 3.46), a mean syntax score of 18.50 (SD 2.8), a mean Token Test score of 23.55 (SD 5.52), and 30% of the patients had a high ASRS rating. A 3-level disorder was found in approximately 39% of the patients; these patients had a mean score for semantics of 13.88 (SD 5.08), for phonology 11.60 (SD 5.33), and for syntax 12.58 (SD 4.86). This group of patients had a mean Token Test score of 10.06 (SD 6.89) and only 26.3% had a high ASRS rating.

Twenty-five patients did not have a disorder on any of the linguistic components. All had been judged as aphasic by their neurologist and speech-language therapist. The Token Test classified 8 of these patients as aphasic; according to the ASRS rating 17 were aphasic, whereas according to the overall score of the ScreeLing 1 patient was aphasic. Four did not have aphasia according to any of these measures.

Table 5. Frequency of Linguistic Disorders (n = 141)

	n (%)
Selective semantic deficit	4 (2.7)
Selective phonological deficit	24 (16.3)
Selective syntactic deficit	5 (3.4)
Semantic and phonological deficit	2 (1.4)
Semantic and syntactic deficit	4 (2.7)
Phonological and syntactic deficit	20 (13.6)
Semantic, phonological, and syntactic deficit	57 (38.8)

Relationship between Linguistic-Level Deficits and Aphasia Severity

There was an overall significant difference (p < 0.001) in aphasia severity, measured by the Token Test, between the subgroups of patients with a selective phonological deficit, a combined phonological and syntactic deficit, and a 3-level deficit (one-way ANOVA analysis). Patients with a 3-level disorder were the most severe (p < 0.001). Their mean Token Test score was significantly lower than the mean Token Test score of the patients with a selective phonological disorder (mean difference = -17.13, 95% CI = -20.94 to -13.33) and of the patients with a combined phonological and syntactic disorder (mean difference = -13.49, 95% CI = -17.50 to -9.48). There was no difference in mean Token Test score between the patients with a selective phonological disorder and a combined disorder.

The subgroups of patients with a selective phonological deficit, a combined phonological and syntactic deficit, and a 3-level deficit, showed an overall significant difference in the ASRS rating with the Kruskal-Wallis test (χ^2 = 30.50, df = 2, p < 0.001). The selective phonological disorder group showed that more patients had high ASRS ratings than in the group with a combined phonological and syntactic disorder (Mann-Whitney tests, Z = -3.30, p = 0.001), and the 3-level disorder group (Z = -5.39, p < 0.001). There was no difference in ASRS ratings between the patients with a combined disorder and a 3-level disorder.

Semantic, phonological, and syntactic scores explained 56.3% of the variance of the ASRS in ordinal regression analysis. Semantics and syntax did not contribute significantly to this effect: phonology alone explained 54.6% of the variance.

DISCUSSION

The ScreeLing proved to be a valid and reliable measure for assessing semantic, phonological, and syntactic deficits in acute aphasia after stroke. Selective linguistic-level disorders occurred in 22.4% of the aphasic patients with phonology as most frequently affected. The importance of assessing the 3 linguistic components separately was further underlined by the finding that they had a different impact on verbal communication, as evaluated with the ASRS. In addition, patients with a selective phonological disorder had the highest ASRS ratings. The number of

linguistic-level disorders was related to the severity of aphasia, measured with the Token Test; patients with impairments on all 3 linguistic components had the lowest Token Test scores.

Our study is the first report on the occurrence of linguistic-level deficits in the acute stage in a large cohort of aphasic stroke patients. In addition, the ScreeLing is the first thoroughly evaluated linguistic-level screening test suitable for assessing the presence and severity of the main linguistic-level deficits in early aphasia. It even exceeds the overall sensitivity and specificity of the well-known Frenchay Aphasia Screening Test (FAST) which was reported to be the best out of 6 aphasia screening tests.[17]

Some aspects of the ScreeLing deserve mention. In the acute stage patients are often too ill to be tested extensively, therefore the ScreeLing has to be short and easy to administer at the bed-side in a hospital as well as in a rehabilitation setting. Another crucial aspect regards the decreasing time of hospitalization: sufficient linguistic information should be available as soon as possible to enable additional targeted assessment for an adequate referral. For each linguistic component, we selected various tasks that optimally capture each linguistic component, as it is not clear which linguistic task best represents language processing at the 3 linguistic components. Not all well-known linguistic tasks appeared to be suitable for the acute stage. For example, we decided not to use non-word repetition even though this is known to represent phonological processing.[18] This task appeared too much of a burden for acute patients.

An earlier research version of the ScreeLing proved to have a high sensitivity (86%) and specificity (96%) in discriminating aphasic and non-aphasic acute stroke patients[12] (see appendix III for the modifications). A limitation of the present study is that we did not examine the discriminative power of the revised ScreeLing in stroke patients with and without aphasia, as our norm group was restricted to healthy controls. Even though this is standard procedure in neuropsychological tests, we will incorporate this aspect in our future research. Another limitation is that our healthy controls were not age-matched and education-matched with the acute and chronic patient groups. In our future research, we will include norm groups of healthy speakers and stroke patients without aphasia who are age-matched and education-matched with the aphasic patients. A final limitation with respect to the psychometric properties of the ScreeLing is the rather low specificity of semantics and syntax. In clinical practice, this would result in a patient being incorrectly classified as having a semantic/ syntactic disorder. It is almost impossible for screening tests to be both highly specific and highly sensitive. We preferred optimal sensitivity in order to avoid misdiagnosing patients with an actual semantic/syntactic disorder.

Our results demonstrate that differential assessment of linguistic-level deficits is feasible at 2 weeks after stroke and that the occurrence of selective linguistic disorders is not rare. A selective semantic disorder was the least frequent and also rarely occurred in combination with just 1 other linguistic-level deficit. This means that if a patient has a deficit in the semantic component, the phonological and/ or syntactical components will also be affected. These findings support the notion that semantics is the central level of language processing and is involved in nearly all aspects of language.[19] Damage to this component is said to affect performance on any task requiring comprehension or production of words.[20]

Interestingly, we found that about 50% of the variance in the ASRS rating was explained by the phonological component alone. This is not in line with previous findings that semantic function contributes more to the variance of verbal communication than phonology.[21-22] These results were obtained in more chronic stages, i.e. 3-5 months[21] and 1-338 weeks[22] after stroke. Verbal communication might be heavily influenced by phonological deficits in the acute stage and more by semantic deficits in the chronic stage. So far, data about the occurrence of linguistic deficits are presently available only for the acute stage.

In a previous pilot study we found that phonology took significantly longer to improve than semantics and syntax, i.e. up to four months after stroke.[23] The present study shows that in acute patients the phonological component is affected most severely and most frequently. Further insight into the recovery course of the 3 linguistic components is needed to evaluate the relevance of our findings for treatment. In a current follow-up study we are investigating the recovery of semantics, phonology, and syntax in the first year after stroke. We will address the occurrence of the linguistic deficits at various time-points and their relation to functional outcome. Furthermore, their additional prognostic value will be investigated.

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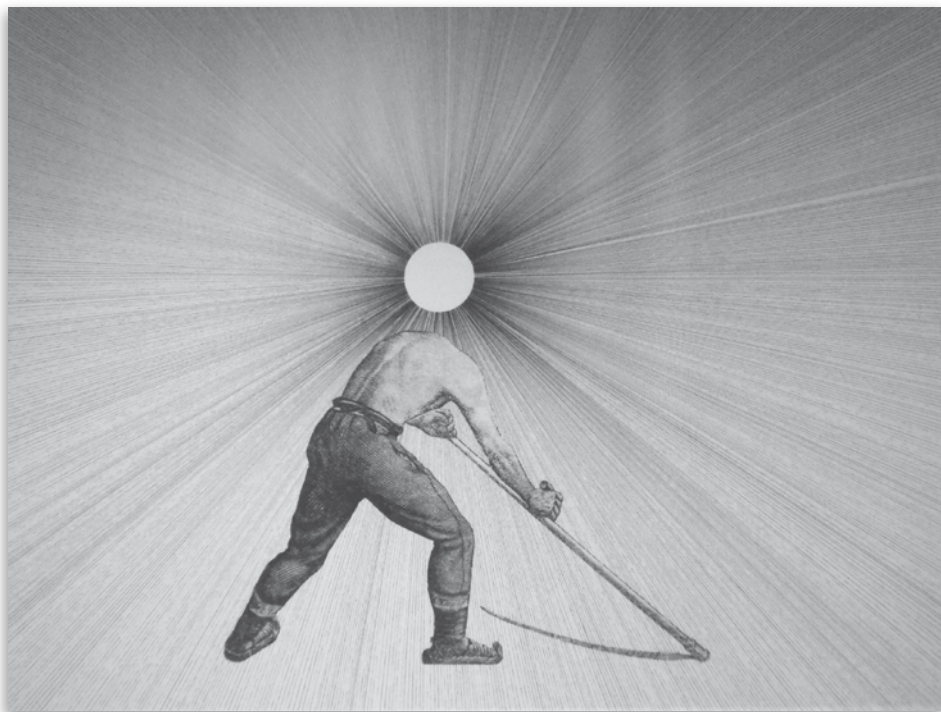
ABSTRACT

Background

The long-term functional outcome of aphasia after stroke is uncertain, even though this information is needed as early as possible for adequate patient care and support.

Objective

This observational prospective study was aimed at predicting functional outcome at 1 year after stroke.

Methods

We examined linguistic components (ScreeLing) and verbal communication (Aphasia Severity Rating Scale, ASRS) in 147 aphasic patients. The ScreeLing was administered at 1, 2, and 6 weeks after stroke; the ASRS at 1 week and 1 year. The relations between linguistic, demographic, and stroke characteristics, and good functional outcome at 1 year (ASRS 4 or 5) were examined with logistic regression analyses.

Results

The baseline linguistic components, i.e. semantics, phonology, and syntax, were significant predictors ($p < 0.001$) for 1 year outcome in univariable analyses. In multivariable analysis, these variables explained 46.5% of the variance with phonology as the only significant predictor ($p = 0.003$). Age, Barthel Index score, education level, and hemorrhagic stroke were identified as other significant predictors of outcome. A prognostic model of these 5 baseline predictors explained 55.7% of the variance. The area under the ROC curve (AUC) was 0.93, indicating good predictive performance. Adding the degree of phonological recovery between 1 week and 6 weeks after stroke to this model increased the explained variance to 65% and the AUC to 0.95.

Conclusion

The outcome of aphasia at 1 year after stroke can be predicted in the first week by the phonology score, the Barthel Index score, age, education level, and stroke subtype, with phonology as the strongest predictor.

INTRODUCTION

Aphasia after stroke has an enormous impact on the quality of life of both the patient and family. Early prediction of verbal outcome of aphasia is crucial for adequate patient care and support.

Over the past years, an increasing number of studies have reported potential prognostic factors for aphasia after stroke[1-3], including age and sex[3], aphasia severity[1,3] and subtype[3], lesion location[4], vascular risk factors such as smoking, and previous cardiovascular disease[5]. Of these factors, the initial aphasia severity is the most robust.[6] The degree of aphasia recovery in the acute stage has also been suggested as a possible prognostic factor.[7] Aphasia subtype, such as Broca or Wernicke, does not predict aphasia outcome.[3]

In the diagnosis and treatment of language disorders in aphasia, the core linguistic components of language production and comprehension, i.e. semantics (word meaning), phonology (word sound), and syntax (sentence structure), are considered to be more important than aphasia subtype.[8] So far, the prognostic relevance of impairments in these linguistic components, which form the basis of adequate verbal communication, has not been investigated.

The aim of this observational prospective follow-up study was to assess potential prognostic factors for the verbal outcome of aphasia at 1 year after stroke, including semantics, phonology, and syntax, and the degree of linguistic recovery in the acute stage.

METHODS

Patients

Between June 2007 and June 2009, a consecutive series of patients with aphasia due to a first-ever stroke were recruited from the stroke units of 17 hospitals in The Netherlands for the Sequential Prognostic Evaluation of Aphasia after stroKe (SPEAK) study. Aphasia was diagnosed by the local neurologist (based on clinical examination) and speech-language therapist (SLT) (based on an interview). Adult Dutch native/near-native speakers who could perform language tests between 2 and 14 days after stroke, and who scored below the cut-off point of the Token Test (i.e. < 29)[9] and/or the ScreeLing (i.e. < 68)[10] were eligible for inclusion. Exclusion criteria were pre-stroke dementia (suspected or confirmed), severe dysarthria (obscuring possible aphasic symptoms), developmental dyslexia, severe impairment of vision and hearing, illiteracy and psychiatric disorder that might interfere with the aphasia assessment.

In this observational prospective follow-up study, all patients were included while admitted to hospital and followed in the subsequent settings, i.e. nursing homes, rehabilitation centers, or at home.

We aimed at a sample size of at least 120 patients to be able to estimate the effect of 12 prognostic variables.[11] Since about 20% of patients with aphasia after stroke die during follow-up[12], we aimed for the inclusion of 150 patients.

The central medical ethics committee of Erasmus MC University Medical Centre and the local ethical committees of the participating centers approved this study. Informed written consent from the patients and/or their close relatives was required.

Assessments

Spontaneous speech was elicited in a 10-minute semi-standardized interview that comprised 4 topics (i.e. the disease, occupation, family and housing, and hobbies), and was evaluated with the Aphasia Severity Rating Scale (ASRS) of the Boston Diagnostic Aphasia Examination (BDAE)[13] as a measure of verbal communication. The BDAE has good reliability[13] and validity[14]. The ASRS is a 6-point scale ranging from 0 'no usable speech or auditory comprehension' to 5 'minimal discernible speech handicap' (see appendix II). This categorical variable was used at 4 days (baseline, T1) and at 1 year after stroke.

The ScreeLing, a screening test for the core linguistic components, was used to detect aphasia in acute stroke patients and to evaluate their performance on semantics (word meaning), phonology (word sound), and syntax (sentence structure).[15] Each linguistic component is examined with 4 well-known tasks: semantic tasks include word-picture matching, identifying semantically anomalous sentences, verbal semantic association, and odd-word out; phonology comprises tasks for repetition, reading aloud, judging same/different spoken word pairs, and matching first phoneme of a spoken word with the grapheme; syntax comprises sentence-picture matching, wh-questions, identifying syntactic incorrect sentences, and sentence completion (see appendix III). Each linguistic component consists of 24 items, with a maximum score of 1 point per item.[10, 16] This test was performed at 4 days (baseline, T1), 12 days (T2), and 6 weeks (T3) after stroke.

All language assessments were conducted by the local SLT's, study coordinator, or test assistants. The study coordinator performed a final check of the results of all assessments. The spontaneous speech samples were scored independently by an experienced speech-language therapist, who was not involved in the assessment or treatment of the patients.

Demographic variables included: age; sex; handedness categorized as 'right-handed', 'not right-handed', or 'unknown'; and education level defined as 'high' (i.e. junior high school or middle vocational education up to university) or 'low' (i.e. unfinished elementary school up to sophomore high school or lower vocational education).

Clinical variables were collected at baseline and included: stroke type categorized as hemorrhage or infarction, the latter subdivided into cardioembolic or non-cardioembolic; and lesion location defined as 'cortical only' versus 'not cortical only' (i.e. sub-cortical only or both cortical and sub-cortical). As a measure of overall stroke-related disability we used the Barthel Index[17] which is a 20-point scale to assess the degree of independence in general daily life activities (e.g. eating, getting dressed). The total number of vascular history variables was analyzed as a continuous variable and included: transient ischemic attack, ischemic heart disease (e.g. myocardial infarction), other heart disease (e.g. valvular), and other vascular disease (e.g. intermittent claudication, amputation). The sum of vascular risk factors was handled as a continuous variable and included: smoking, excessive alcohol use, hypertension, hypercholesterolemia, diabetes mellitus, and atrial fibrillation (Table 1).

All patients were referred for speech-language treatment after T1 according to standard procedure. Treatment did not start before the language assessments at T1 were completed. Treatment comprised a median of 27.5 hours (interquartile range 3-83) during the 1 year follow-up period.

Outcome Measure

We chose verbal communicative ability at 1 year after stroke as outcome measure, which was defined by the ASRS[13] as a dichotomous variable with scores 0-3 indicating poor functional aphasia outcome and scores 4-5 indicating good functional aphasia outcome.

Statistical Analyses

We examined the influence of potential prognostic factors, assessed at baseline, on good functional outcome (i.e. ASRS score 4 or 5) at 1 year after stroke. The first step was to investigate the influence of the linguistic variables, i.e. semantics, phonology, and syntax scores with univariable logistic regression analyses. Then, the combined influence of the linguistic variables on good outcome was investigated in multivariable logistic regression analysis. Next, we investigated the influence of other potential prognostic factors with univariable logistic regression analyses, selected on the basis of the literature and a priori clinical judgment: age, sex, handedness, education level, stroke subtype, lesion location, Barthel Index score, vascular history, and other risk factors. Variables (linguistic and others) with a p value ≤ 0.20 were entered in the final multivariable model. The predictive accuracy of this final baseline model was determined by means of Receiver Operating Characteristic (ROC) analysis and the explained variance (R^2).

In exploratory analyses we investigated whether the degree of aphasia recovery in the acute stage (i.e. between baseline (T1) and 12 days (T2), and between baseline (T1) and 6 weeks (T3)) had additional prognostic value compared with the baseline model.

The extrapolation method was used for missing values of the ASRS at 1 year after stroke in patients who already had obtained score 4 or 5 at previous assessments. All analyses were completed using SPSS version 15.0.

RESULTS

We included 147 patients. Their baseline characteristics are shown in Table 1.

Table 1. Baseline Characteristics of the 147 Included Patients

Demographical	
Age, years, mean (SD)	67 (15)
Female sex, *n (%)*	78 (53)
Handedness, *n (%)*	
Right-handed	127 (86)
Not right-handed (i.e. left or ambidextrous)	17 (12)
Unknown	3 (2)
Level of education, *n (%)*	
High[a]	73 (50)
Low[b]	69 (47)
Unknown	5 (3)

Table 1. Baseline Characteristics of the 147 Included Patients – *continued*

Neurological	
Clinical localization of stroke, *n (%)*	
Left hemisphere	145 (99)
Right hemisphere	2 (1)
Stroke subtype, *n (%)*	
Infarction	126 (86)
Non-cardioembolic	84 (57)
Cardioembolic	42 (29)
Intracerebral hemorrhage	21 (14)
Lesion location, *n (%)*	
Cortical only	64 (51)
Not cortical only[c]	15 (12)
No visible lesions	47 (37)
Barthel Index at T1[d] (0-20), median (interquartile range)	15 (8-20)
Risk factors	
Vascular history, *n (%)*	
Ischemic heart disease	32 (22)
Other heart disease	14 (10)
Other vascular disease	12 (8)
Transient Ischemic Attack	16 (11)
Vascular risk factors, *n (%)*	
Current smoking	54 (37)
Excessive alcohol use	4 (3)
Hypercholesterolemia	37 (25)
Hypertension	64 (44)
Diabetes mellitus	15 (10)
Atrial fibrillation	34 (23)
Linguistic performance (ScreeLing)[10]	
Semantics at T1[d] (0-24), mean (SD)	17 (6)
Phonology at T1[d] (0-24), mean (SD)	14 (6)
Syntax at T1[d] (0-24), mean (SD)	15 (6)

SD, standard deviation.
[a] Junior high school or middle vocational education up to university.
[b] Unfinished elementary school up to sophomore high school or lower vocational education.
[c] That is sub-cortical only or both cortical and sub-cortical.
[d] Mean days after stroke at T1 was 4.

In 32 patients the 1 year follow-up could not be completed due to death (n = 11), serious concomitant illness (n = 8), refusal to further participate (n = 12), and

emigration (n = 1). Of these patients, 15 already had obtained score 4 or 5 on the ASRS at previous assessments and these observations were extrapolated to the 1 year time point. Data for the remaining 17 patients could not be extrapolated because they had not obtained score 4 or 5 at previous assessments. A total of 130 patients were entered into the prognostic analyses. We conducted the analyses also without the extrapolated data of the 15 patients and obtained the same results. At baseline (4 days), 22% had a score of 4 or 5 on the ASRS, and at 1 year 80%. Figure 1 displays the full distribution of the ASRS at baseline and at 1 year after stroke.
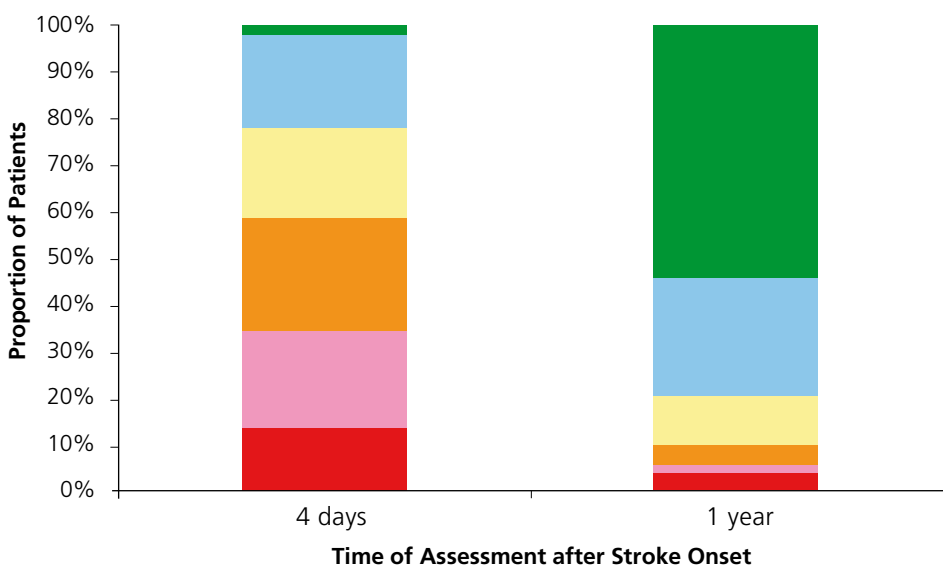
score 0, no usable speech or auditory comprehension (red bar); score 1, communication through fragmentary expression (pink bar); score 2, conversation about familiar subjects is possible with help (orange bar); score 3, conversation about everyday problems is possible with (almost) no help (yellow bar); score 4, obvious loss of fluency or facility of comprehension (blue bar); score 5, minimal discernible speech handicap (green bar).

Figure 1. Distribution of the Aphasia Severity Rating Scale (ASRS)

Prediction of Aphasia Outcome

The 3 baseline linguistic component scores were associated with functional outcome at 1 year after stroke. These baseline scores explained 46.5% of the variance in multivariable analysis, with phonology as the only significant predictor (Table 2).

Age, Barthel Index score, education level, and stroke subtype were the other significant independent predictors with a p value ≤ 0.20 in univariable logistic regression analyses (Table 2).

Our final multivariable regression model consisted of the phonology score, Barthel Index score, age, education level, and stroke subtype. This model explained 55.7% of the variance (Table 2) and showed good discriminative ability with an AUC (area under the receiver operating characteristic curve) of 0.93.

Table 2. Baseline Predictors of Good[a] Aphasia Outcome at 1 Year after Stroke in 130 Patients

	R^2	OR for Good[a] Outcome (95% CI)
Univariable analyses		
Linguistic variables		
Semantic score at T1[b]	34.5%	1.24 (1.13-1.36)
Phonology score at T1[b]	44.9%	1.33 (1.18-1.49)
Syntax score at T1[b]	33.2%	1.24 (1.13-1.36)
Barthel Index score at T1[b] (0-20)	24.4%	1.17 (1.09-1.26)
Age at T1[b] (19-96)	5%	0.97 (0.93-1.00)
Education level	6.4%	
High[c]		1 (reference)
Low[d]		0.34 (0.13-0.89)
Stroke subtype	5.1%	
Non-cardioembolic infarction		1 (reference)
Cardioembolic infarction		0.70 (0.27-1.82)
Intracerebral hemorrhage		4.43 (0.55-35.96)
Multivariable analyses		
Linguistic model	46.5%	
Semantics score at T1[b]		1.08 (0.93-1.27)
Phonology score at T1[b]		1.28 (1.09-1.50)
Syntax score at T1[b]		0.98 (0.82-1.18)
Final model	55.7%	
Phonology score at T1[b] (0-24)		1.31 (1.15-1.51)
Barthel index at T1[b] (0-20)		1.11 (1.00-1.21)
Age at T1[b] (19-96)		0.94 (0.89-0.99)
Education level		
High[c]		1 (reference)
Low[d]		0.47 (0.12-1.84)
Stroke subtype		
Non-cardioembolic infarction		1 (reference)
Cardioembolic infarction		1.31 (0.29-5.92)
Intracerebral hemorrhage		8.85 (0.70-111.28)

R^2, explained variance; OR, odds ratio; CI, confidence interval.
[a] Good aphasia outcome was defined as score 4 or 5 on the Aphasia Severity Rating Scale.
[b] Mean days after stroke at T1 was 4.
[c] Junior high school or middle vocational education up to university.
[d] Unfinished elementary school up to sophomore high school or lower vocational education.

Adding the degree of phonological recovery between baseline (T1) and 6 weeks (T3) to the final model increased the explained variance to 65% (Table 3) and the AUC to 0.95.

Table 3. Additional Prognostic Value of the Degree of Recovery

	AUC	R^2	OR for Good[a] Outcome (95% CI)[b]
Baseline predictors[c] + recovery between T1[d] and T2[e]	0.95	62%	
Δ phonology score (score T2[e] - score T1[d])			1.25 (1.00-1.57)
Baseline predictors[c] + recovery between T1[d] and T3[f]	0.95	65%	
Δ phonology score (score T3[f] - score T1[d])			1.25 (0.98-1.61)

AUC, area under the receiver operating characteristic curve; R^2, explained variance; OR, odds ratio; CI, confidence interval.
[a] Good aphasia outcome was defined as score 4 or 5 on the Aphasia Severity Rating Scale.
[b] Multivariable odds ratio adjusted for phonology at baseline, Barthel Index, age, education level, and stroke subtype.
[c] Baseline predictors: phonology, Barthel Index, age, education level, and stroke subtype.
[d] Mean days after stroke was 4.
[e] Mean days after stroke was 12.
[f] Mean days after stroke was 43.

The probability of good aphasia outcome at 1 year after stroke can be calculated within the first 6 days based on the regression coefficients of the baseline multivariable model (Table 4). For example, a patient aged 59, with a low level of education, admitted to the stroke unit with a cardioembolic infarction, and assessed within 6 days after stroke with a phonology score of 6, and a Barthel Index score of 14, would have a probability of 0.74 to have a good aphasia outcome at 1 year after stroke.

Table 4. Logistic Regression Model for the Probability of Good[a] Aphasia Outcome at 1 Year after Stroke

Baseline Prognostic Variables	Value	Regression Coefficient
Phonology score at T1[b]	0-24	$C_1 = 0.27$
Barthel Index score at T1[b]	0-20	$C_2 = 0.10$
Age at T1[b]	19-96	$C_3 = -0.06$
Education level (high[c] = 0; low[d] = 1)	1 or 0	$C_4 = -0.76$
Stroke subtype		
Non-cardioembolic infarction	0	
Cardioembolic infarction	1 or 0	$C_5 = 0.27$
Intracerebral hemorrhage	1 or 0	$C_6 = 2.18$
Constant		$C_0 = 2.04$

$$p \text{ (ASRS 4 or 5)} = \frac{e^y}{1 + e^y}; \ y = C_0 + C_1 \text{ (phonology score)} + C_2 \text{ (Barthel Index score)} + C_3 \text{ (age)} + C_4 \text{ (education level)} + C_5 \text{ (cardioembolic infarction)} + C_6 \text{ (hemorrhage)}$$

ASRS, Aphasia Severity Rating Scale.
[a] Good aphasia outcome was defined as score 4 or 5 on the Aphasia Severity Rating Scale.
[b] Mean days after stroke was 4.
[c] Junior high school or middle vocational education up to university.
[d] Unfinished elementary school up to sophomore high school or lower vocational education.

DISCUSSION

This study shows that verbal outcome of aphasia can be predicted as early as the first week after stroke by the phonology score, the Barthel Index score, age, education level, and stroke subtype. Phonology proved to be the strongest linguistic predictor, which emphasizes the importance of investigating the core linguistic components in the acute stage. We constructed a prognostic model which showed good discriminative ability. The addition of recovery of phonological processing between 4 days and 6 weeks after stroke to the baseline model further improved its prognostic value.

Strengths of our study are that it is the first report on the predictive value of the main linguistic components in a large cohort of aphasic patients ranging from very mild to very severe aphasia, with a 1 year follow-up and frequent assessments in the acute stage. Previous studies used general aphasia measures, and either conducted a baseline assessment and 1 follow-up assessment[1, 3] or focused on a shorter follow-up period with more frequent observations[7]. Our proportion of missing data (21.8%) can be considered small compared with a recent prognostic study that reported nearly 40% of missing outcome at 6 months after stroke[5]. Missing data are common and unavoidable in this type of study, since stroke patients are at high risk for death and concomitant illness.

Our study has some limitations. First, we had to dichotomize our outcome variable because in the more severe categories of the ASRS we lacked adequate numbers of patients, which precluded the use of ordinal regression models (shift analysis). We report that 80% of our cohort had a good aphasia outcome at 1 year after stroke, defined as a score of 4 (mild aphasia) or 5 (no aphasia) on the ASRS. Other studies defined good aphasia outcome as complete recovery resulting in a lower prevalence of recovery.[3, 7] Second, the 3 core linguistic components were not examined extensively, but with a screening tool. The ScreeLing examines each linguistic component with 4 short tasks that are specific for semantic, phonological, and syntactic processing. It can be easily used in acute patients, which is important as these patients cannot undergo extensive test batteries. However, considering the prognostic relevance of phonology, more detailed information about the nature of the phonological deficit might refine its predictive power. In addition, it is important to realize that the focus of this study is verbal communication. The results do not allow predictions of outcome in other language functions, such as reading and writing, nor in the way the aphasic symptoms influence daily life functioning. Finally, we were unable to incorporate the role of structural brain damage in our prognostic model. Because of the observational design of our study data from routine CT scanning was not adequate. We did not conduct serial CT scanning which could have provided us with specific information on the size and location of the lesion and their impact on the prognosis of aphasia after stroke.

It is intriguing that phonology proved to be the strongest predictor of the 3 linguistic components, which might be related to differences in lateralization. Recently it has been reported in a meta-analysis that semantic and syntactic processing activates both the right and left hemisphere, while phonological processing is more unilaterally localized in the left hemisphere.[18] This might explain the key role of phonology in our study, since our cohort almost entirely consists of patients with lesions in the left hemisphere. Even though this is all highly speculative, this seems to be supported by the finding that phonological processing has the longest recovery period in

comparison with semantic and syntactic processing.[19] However, this should be explored in future fMRI studies. Our finding of the initial severity of the phonological impairment as a relevant prognostic factor for good aphasia outcome is consistent with other studies that used more general aphasia assessments.[1, 3, 7] The reported explained variances of previous prognostic models (50%-60%)[1, 7] are comparable with the explained variance of our model (55.7%), except for 1 small study (n = 21) that reported an explained variance of 81%[1]. However, this study used as outcome variable the achieved change in language score: achieved score minus initial score, which is dependent on the predictor, i.e. initial language score.[1] Therefore these results should be interpreted with caution. Other differences with our study are that the authors[1] used 3 months as principle endpoint and excluded patients with severe aphasia[20].

Our results confirm the notion that information on recovery rate will improve prognostic accuracy.[7] The recovery of the phonological component between baseline and 6 weeks after stroke added 9.3% of explained variance to the baseline model. Whether the rate of recovery during this period was influenced by treatment, was beyond the scope of this observational study, similar to several other recent studies[1, 5]. Given the observational nature of our study we did not aim to influence therapy. The patients were treated in different centers all over the Netherlands, which resulted in a great variation in the speech-language therapy they received. No specific data were available about the amount of cognitive linguistic therapy directed at the main linguistic components.

In line with other studies of large cohorts of patients with aphasia we identified stroke-related disability, assessed with the Barthel Index, as a relevant prognostic factor as well.[3, 7] Only 1 earlier study found a significant effect for age[12], contrary to others[1, 3, 7]. A possible explanation is the difference in mean age between the studies, i.e. 59[1] to 76 years[3, 7], and specifically the difference in the range of the included ages (SD's varying from 9[7] to 15 in our study). Our data differ from 2 studies that have investigated the predictive value of education in which no effect of education on aphasia outcome was observed.[2, 21] These studies examined small cohorts of patients. Consistent with other studies, we found no effect of sex, handedness, lesion location, vascular history, and other risk factors.[2, 7]

The formula derived from the regression coefficients of our baseline model might be used in stroke units given that information on most of our predictors (e.g. stroke subtype) are readily available, since this is standard practice in the acute stage after stroke, and phonological processing and stroke-related disability (Barthel Index) can be easily assessed. If our findings are confirmed after external validation, a clinical prognostic tool, a score chart, may be constructed for use in the acute stage. The benefit of such an early prediction is that patients can be more adequately informed about what to expect of their future verbal communication. The external validity of the model in terms of the influence of aphasic symptoms on daily life disability should be explored in future studies.

In summary, we identified predictors of verbal outcome of aphasia at 1 year after stroke and constructed a multivariable model as potential clinical tool for early prediction. Our finding that of the core linguistic components, i.e. semantics, phonology, and syntax, the initial severity of the phonological disorder was the strongest predictor indicates that a careful assessment of specific linguistic characteristics of aphasia early after stroke is recommended.

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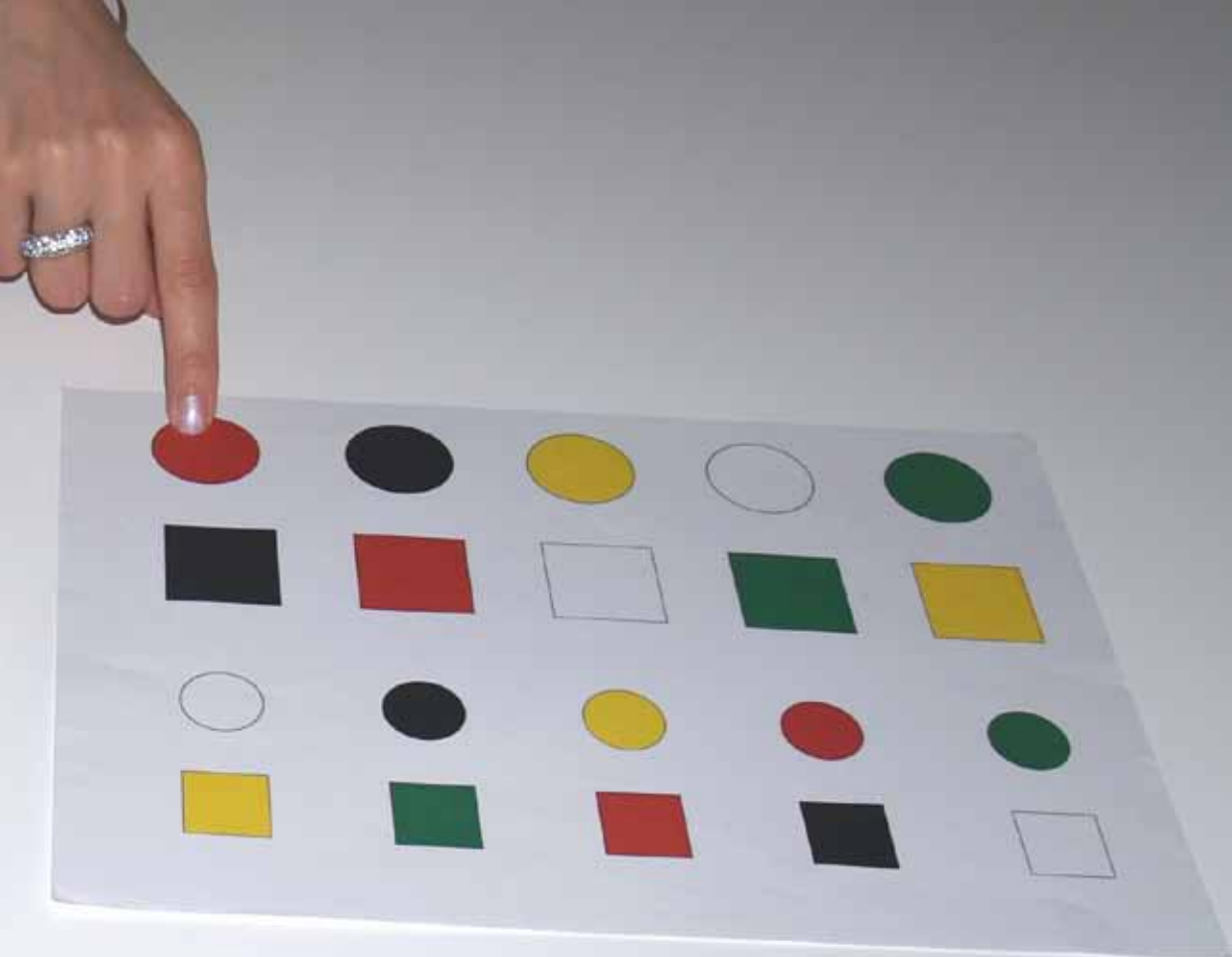
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**RECOVERY OF
APHASIA AFTER STROKE:
A 1-YEAR FOLLOW-UP STUDY**

ABSTRACT

Background

Semantics, phonology, and syntax are essential elements of aphasia diagnosis and treatment. Until now, these linguistic components have not been specifically addressed in follow-up studies of aphasia recovery after stroke.

Objective

The aim of this observational prospective follow-up study was to investigate semantic, phonological, and syntactic recovery in aphasic stroke patients. In addition, we investigated the recovery of verbal communication and of aphasia severity.

Methods

We assessed 147 aphasic patients at 1, 2, and 6 weeks, 3 and 6 months, and 1 year after stroke with the ScreeLing, a screening test for detecting deficits in the 3 main linguistic components, the Aphasia Severity Rating Scale (ASRS), a measure of verbal communication, and the Token Test, a measure of aphasia severity. We investigated the differences in scores between the 6 time points with mixed models.

Results

Semantics and syntax improved up to 6 weeks ($p < 0.001$) after stroke, and phonology up to 3 months ($p \leq 0.001$). ASRS improved up to 6 months ($p < 0.05$) and the Token Test up to 3 months ($p < 0.001$).

Conclusion

We conclude that in aphasia after stroke, various linguistic components have a different recovery pattern, with phonology showing the longest period of recovery that paralleled aphasia severity, as measured with the Token Test. The improvement of verbal communication continues after the stabilization of the recovery of the linguistic components.

INTRODUCTION

Recovery of aphasia after stroke has been investigated in several studies.[1-4] The reported period of aphasia recovery varies from 2 weeks[3] to 1 year[4], and occurs mainly within the first 3 months after stroke onset[1-3]. Previous recovery studies have used overall measures, such as a stroke subscale for aphasia severity[3], measures of verbal communication[2], and general aphasia test batteries[1-2], but have not addressed the core linguistic components of verbal communication i.e., semantics, phonology, and syntax. These linguistic components are the basis for cognitive-linguistic diagnosis and treatment[5] which is commonly applied by speech-language therapists. Insight into the recovery process of semantics, phonology, and syntax, is important for rehabilitation planning and may in the long-run improve aphasia outcome. In a pilot study (n = 15), we have investigated the recovery of individual linguistic components, and have found that it is valuable to investigate aphasia recovery in more detail as the linguistic components did not recover simultaneously.[6] The recovery of phonological impairment took longer, i.e. up to 4 months, than semantic and syntactic impairment which both improved up to 7 weeks after stroke.[6] If confirmed, this finding may have implications for selecting and timing of specific linguistic treatment programs during the rehabilitation course.

The aim of this observational prospective follow-up study was to investigate the recovery pattern of the core linguistic components in patients with aphasia after stroke. In addition to semantics, phonology, and syntax, we investigated the recovery of verbal communication and of aphasia severity.

METHODS

Patients

The Sequential Prognostic Evaluation of Aphasia after stroKe (SPEAK) cohort includes a consecutive series of adult Dutch native/near-native speakers with aphasia due to a first-ever stroke recruited from stroke units between June 2007 and June 2009. The inclusion and exclusion criteria have been described in detail.[7] All patients were included while admitted to hospital and followed in the subsequent settings, i.e. nursing homes, rehabilitation centers, or at home.

The medical ethics committees of Erasmus MC University Medical Center and of the local participating centers approved this study. Informed written consent was required from the patients and/or their close relatives.

Assessments

Six assessments were conducted: at 2-6 days (T1), 7-14 days (T2), 6 weeks (T3), 3 months (T4), 6 months (T5), and at 1 year after stroke (T6). Each assessment included the following 3 measures:
  1. The ScreeLing, a screening test to detect aphasia in acute stroke patients and to assess their functioning on the main linguistic components, i.e. semantics, phonology, and syntax Each linguistic component is examined with 24 items with a maximum total score of 24 (see appendix III).[7-8] The ScreeLing and its

3 linguistic components correlates significantly with the Token Test[9], indicating good concurrent validity[7].

2. Spontaneous speech, as a measure of verbal communication, was elicited in a 10-minute semi-standardized interview with 4 topics: the beginning and course of the disease (e.g. 'Could you tell me how you became ill?'); occupation; family and housing conditions; and hobbies, and evaluated with the Aphasia Severity Rating Scale (ASRS) of the Boston Diagnostic Aphasia Examination[10]. It is a 6-point scale ranging from 0 'no usable speech or auditory comprehension' to 5 'minimal discernible speech handicap' (see appendix II).

3. The Token Test (36 items-version), measures the presence and severity of aphasia.[9]

All language assessments were conducted by the local speech-language therapists (SLT's), study coordinator, or test assistants. The study coordinator performed a final check of the results of all assessments. The spontaneous speech samples were scored independently by an experienced speech-language therapist, who was not involved in the assessment or treatment of the patients. The local SLT's were trained by the study coordinator to administer all language tests during a workshop session organized in each participating region. A manual of the language assessments and the score forms were send to the SLT's beforehand. Most of the speech-language therapists were already familiar with the Token Test and the semi-standardized interview. All SLT's had to administer and tape-record 1 trail assessment before the start of patient inclusion. This trail assessment was scored by the study coordinator who then gave feedback to the SLT's. The test assistants were trained in one-to-one sessions with the study coordinator and by observing the study coordinator while testing patients.

The SLT's registered duration, amount, and content of therapy for each patient during the 1-year-follow-up period.

Statistical Analyses

We established the recovery pattern of each linguistic component, i.e. semantics, phonology, and syntax, the ASRS, and the Token Test by investigating the differences in scores between the 6 assessments, taking the different time frames between the assessments into account, with ordinal (for the ordinal ASRS) and linear (for the continuous ScreeLing and Token Test) mixed models with Bonferroni correction for multiple testing. No imputations were made for missing data; those without an assessment score were excluded.

In exploratory analyses we established the recovery pattern of patients who did not receive therapy and of those that did receive therapy. We further compared their baseline scores of the linguistic components, the ASRS, and the Token Test with Mann-Whitney tests.

All analyses were completed using SPSS version 15.0 or R statistical software version 2.7.

RESULTS

The demographic and clinical characteristics of the 147 included patients are summarized in Table 1.

Table 1. Demographic and Clinical Characteristics of the Included Patients

Age, years, mean (SD)	67 (15)
Sex, male/female, *n*	69/78
Handedness, *n (%)*	
Right-handed	127 (86)
Left-handed	15 (10)
Ambidextrous	2 (1)
Unknown	3 (2)
Clinical localization of stroke, *n (%)*	
Left hemisphere	145 (99)
Right hemisphere	2 (1)
Stroke type, *n (%)*	
Cerebral infarction	126 (86)
Intracerebral hemorrhage	21 (14)

SD, standard deviation.

The follow-up at 1 year could not be completed in 32 patients for the following reasons: death (n = 11), serious concomitant illness (n = 8), refusal to further participate (n = 12), and emigration (n = 1). In 15 patients only one of the assessments was missing, mainly the first (n = 7), due to illness of the patient (n = 5) or absence of the speech-language therapist (n = 2). The number of patients assessed at each time point and the time elapsed after stroke are summarized in Table 2.

A total of 24 patients did not receive speech-language therapy because of early recovery (n = 21), or refusal (n = 3), and for 5 patients we could not ascertain whether or not they received therapy because of early refusal to further participate in the study. For 23 patients it was reported that they received therapy, but information on the duration, amount, and content of therapy was not registered. The other 95 patients received a median of 15 hours (interquartile range (IQR) 1-34) of speech-language therapy in the acute and post-acute stage (i.e. within 3 months after stroke onset). The therapy started in the first week after stroke for 18 of these patients, between 1 week and 15 days for 20 patients, between 16 and 30 days for 33 patients, and after 1 month for 24 patients. In 78 patients therapy was continued after 3 months; they received a median of 1 hour (IQR 0-46) of therapy in the chronic stage (i.e. between 3 months and 1 year after stroke). The therapy content and intensity provided by the SLT's showed a great variation among and within patients. Therefore, we are unable to report on the specific content and intensity of therapy.

Table 2. Time of Assessment after Stroke in Days and Number of Patients Assessed

| Assessment	T1	T2	T3	T4	T5	T6
N	136	144	135	125	120	115
Time after stroke in days (SD)	4 (1.5)	12 (2.1)	43 (2.5)	92 (5.8)	187 (9.5)	372 (22)

SD, standard deviation.

Group Results

Patients improved on semantics and syntax between T1 (2-6 days) and T2 (7-14 days) (mean difference = 2.3, p < 0.001), and between T2 (7-14 days) and T3 (6 weeks) (mean difference = 1.8, p < 0.001). For phonology, improvement was found between T1 (2-6 days) and T2 (7-14 days) (mean difference = 2.8, p < 0.001), between T2 (7-14 days) and T3 (6 weeks) (mean difference = 1.8, p < 0.001), and between T3 (6 weeks) and T4 (3 months) (mean difference = 1.0, p = 0.001) (Figure 1).
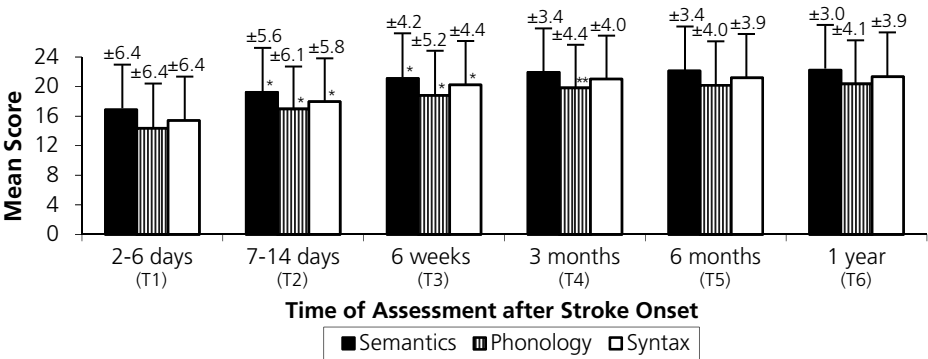
*Significant improvement in relation to the preceding assessment p < 0.001; **p = 0.001 (linear mixed models).
T Standard deviation.

**Figure 1.** Recovery on the Linguistic Components (maximum score 24)
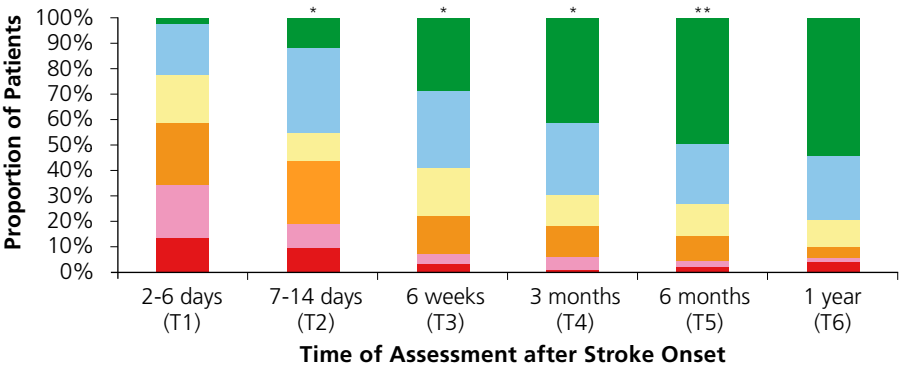
score 0, no usable speech or auditory comprehension (red bar); score 1, communication through fragmentary expression (pink bar); score 2, conversation about familiar subjects is possible with help (orange bar); score 3, conversation about everyday problems is possible with (almost) no help (yellow bar); score 4, obvious loss of fluency (blue bar); score 5, minimal discernible speech handicap (green bar).

*Significant improvement in relation to the preceding assessment p < 0.001; **p = 0.02 (ordinal mixed models).

Figure 2. Recovery on the Aphasia Severity Rating Scale (ASRS)

Patients showed improvement in verbal communication measured with the ASRS between: T1 and T2 (p < 0.001); T2 and T3 (p < 0.001); T3 and T4 (p < 0.001); and T4 and T5 (p = 0.029) (Figure 2).

The Token Test scores improved between T1 and T2 (mean difference = 3.9, p < 0.001), between T2 and T3 (mean difference = 4.4, p < 0.001), and between T3 and T4 (mean difference = 1.8, p < 0.001) (Figure 3).
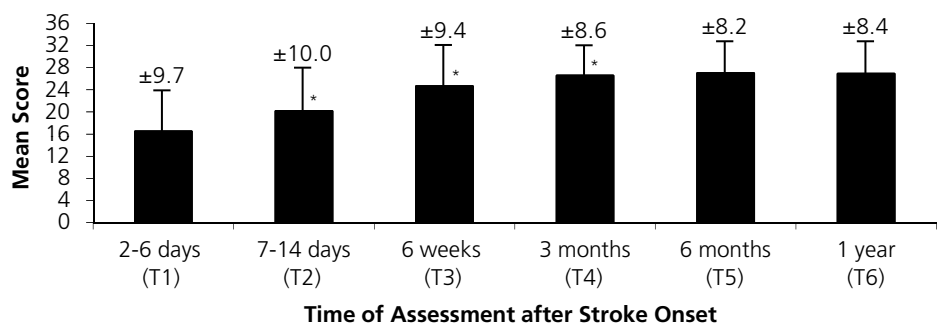
*Significant improvement in relation to the preceding assessment p < 0.001 (linear mixed models).
T Standard deviation.

Figure 3. Recovery on the Token Test (maximum score 36)

Therapy versus No-Therapy

The therapy group showed the same recovery pattern as the complete group. The small group of patients who did not receive therapy showed a different pattern. No improvement was found for semantics. Between T1 and T2 improvement was found on phonology (p < 0.001) and syntax (p = 0.017). Patients showed improvement on the ASRS between T1 and T2 (p < 0.001). On the Token Test improvement occurred between T1 and T2 (p = 0.001) and between T2 and T3 (p = 0.039). The patients with no therapy had higher baseline scores than the therapy group: mean semantics score 19.6 (SD 6.1), mean phonology score 17.8 (SD 5.9), mean syntax score 19.0 (SD 6.2), median ASRS 4 (IQR 2-4), and mean Token Test score 23.4 (SD 8.0) versus mean semantics score 16.6 (SD 6.3) (p = 0.016), mean phonology score 13.7 (SD 6.2) (p = 0.002), mean syntax score 14.8 (SD 6.2) (p = 0.001), median ASRS 2 (IQR 1-3) (p = 0.001), and mean Token Test score 15.1 (SD 9.5) (p < 0.001).

DISCUSSION

Our study shows that in patients with aphasia after stroke, semantics, phonology, and syntax do not recover simultaneously. Semantics and syntax improved significantly up to 6 weeks. Phonology and the Token Test scores showed a longer period of recovery, up to 3 months, in line with the prolonged recovery of verbal communication, which reached a plateau at 6 months after stroke.

This is the first report on the recovery of the main linguistic components in a large cohort of aphasic stroke patients. In addition, the long follow-up period combined with frequent assessments, particularly in the acute stage, is unique. So far, aphasia recovery studies have aimed at either a longer follow-up period[2, 4] or at frequent assessments in the acute stage[1, 3].

There is large interest in the effect of speech-language therapy on linguistic recovery. In our observational study, patients were treated according to the local procedures in the participating centers in the Netherlands; we did not influence therapy. We observed large differences in the content, intensity, and duration of therapy, and found that patients with high linguistic baseline scores were less likely to receive therapy. This 'confounding by indication' (only patients who need treatment are treated) is a common epidemiological problem and makes it impossible to draw conclusions on treatment effects from observational studies. We observed a shorter recovery period in the small group of patients that did not receive therapy, which we expect to be due to their high baseline scores and early spontaneous recovery. In other recent studies on aphasia after stroke, speech-language therapy was not monitored at all.[11-12]

The current data confirm the results of our pilot study.[6] Semantics and syntax both showed the shortest period of recovery. The longer recovery period of phonology illustrates a different involvement of the linguistic components in the recovery process. We cannot rule out or confirm that this difference in recovery pattern of the linguistic components is related to treatment variables, given the great variation in the content, intensity, and the start of therapy. The improvement on the Token Test, which parallels the final recovery stage of the linguistic components, emphasizes the importance of these components for the recovery process. Adequate verbal communication in a pragmatic setting requires a dynamic interaction between semantics, phonology, and syntax in combination with the intended information load. The recovery of verbal communication, as measured with the ASRS, exceeded the time span of the recovery of all 3 linguistic components. In a long-term follow-up study of a case with global aphasia, verbal communication was also the latest modality to recover.[13]

In line with other observational studies on large cohorts of patients with severe as well as mild aphasia, we found no further improvement beyond 3 months after stroke on all except one (ASRS) of our language measures.[2-3] Several studies report on improvement in language function in the chronic stage following speech-language therapy.[14] The lack of further improvement in our cohort may be explained by the fact that our study was not designed to study treatment effects, by a ceiling effect, and by the relatively low intensity of speech-language therapy in the chronic stage.

The implications of our results for the treatment of aphasia in the first 3 months after stroke onset are as yet unclear and need to be investigated further. Very early and intensive cognitive linguistic therapy[5] may reinforce the natural recovery of semantics, phonology, and syntax. Alternatively, it could be better to postpone the start of therapy until after the recovery process has stopped. A recent randomized controlled trial on the efficacy of cognitive linguistic therapy and communicative therapy did not conclusively prove that cognitive linguistic therapy is effective in the early stage after stroke.[15]

In this study, we did not investigate the neural mechanisms of the recovery of the linguistic components, which are assumed to be different for each component.[16] Future research incorporating fMRI scanning during follow-up could result in more insight into the underlying process of the recovery of the linguistic components. In addition, we did not incorporate the impact of structural brain damage on the recovery of aphasia. Serial CT scanning could have provided us with specific information on the size and location of the lesion, and their role in aphasia recovery.

To conclude, phonology showed a longer recovery period than semantics and syntax in stroke patients with aphasia. These findings suggest that evaluating the main linguistic components in aphasia after stroke is useful. Future studies should clarify whether individualized treatment of aphasic stroke patients on the basis of the affected linguistic components improves outcome.

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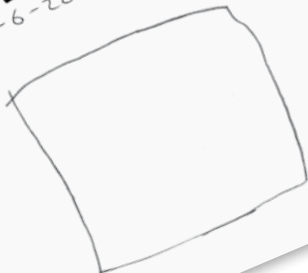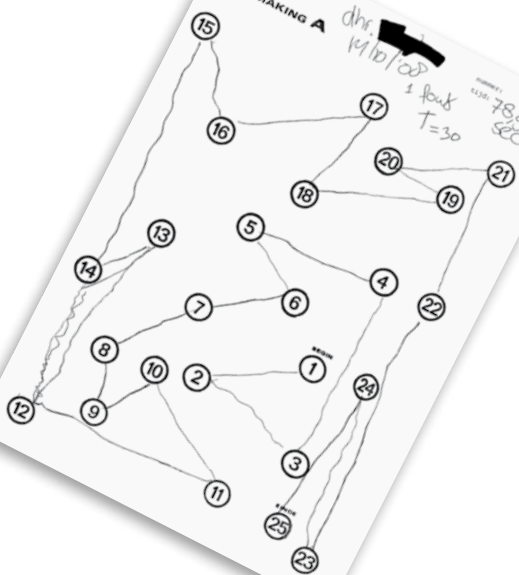
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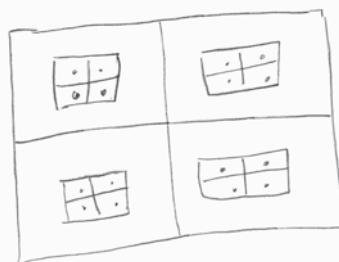
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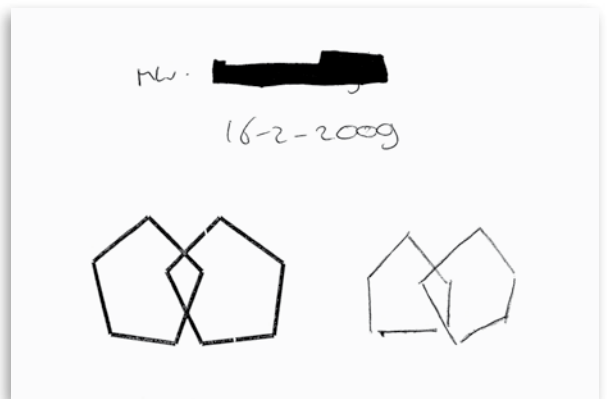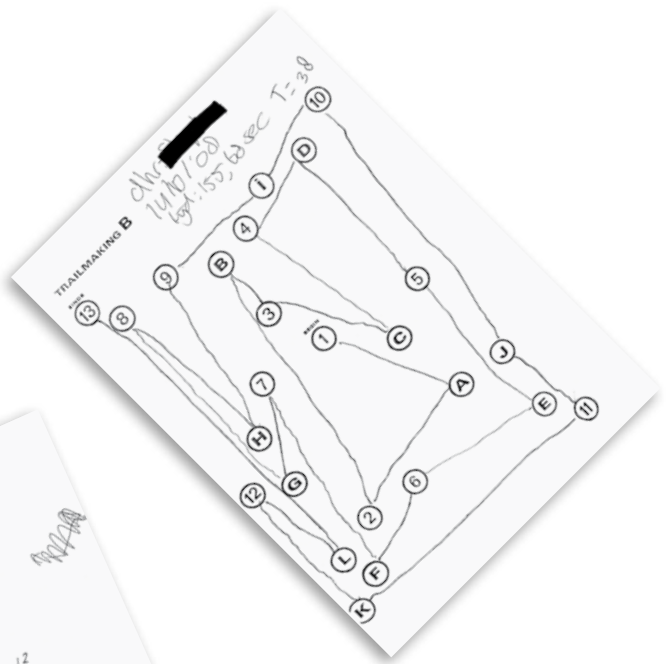
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NON-LINGUISTIC COGNITIVE IMPAIRMENTS IN POST-STROKE APHASIA: A PROSPECTIVE STUDY

ABSTRACT

Background

Information on cognitive impairment in aphasic patients is limited.

Objective

To investigate the prevalence and course of non-linguistic cognitive impairments in the first year after stroke, and their association with aphasia and functional outcome.

Methods

We included 147 patients with acute aphasia. At 3 months and 1 year, we assessed cognition with the MMSE (Mini-Mental State Examination) and with a non-linguistic cognitive examination including abstract reasoning, visual memory, visual perception and construction, and executive functioning. We assessed language with a verbal communication rating (Aphasia Severity Rating Scale), the ScreeLing (a linguistic-level screening test), and the Token Test. We evaluated functional outcome with the modified Rankin scale and we registered the use of anti-depressants.

Results

In total, 107 (88%) patients had impairments in at least 1 non-linguistic cognitive domain at 3 months, and 91 (80%) at 1 year. The most frequently observed impairment concerned visual memory (83% at 3 months; 78% at 1 year) and the least frequent visual perception and construction (19% at 3 months; 14% at 1 year). There was improvement on the MMSE and all cognitive domains including language, except for abstract reasoning. Patients with persisting aphasia had lower cognitive domain scores, worse functional outcome, and were more often depressed than patients who had recovered from aphasia.

Conclusion

Standard non-linguistic cognitive examination is recommended in aphasic stroke patients. Non-linguistic cognitive impairments are common and associated with poor functional outcome and depression, especially in patients with persisting aphasia.

INTRODUCTION

Cognitive impairment is common after stroke[1] and associated with worse recovery[2], dementia[3], worse functional outcome[4], and poor survival[5]. It is also a risk factor for depression and reduced quality of life[6], and hence interferes with the rehabilitation process. One of the most disabling cognitive disorders is aphasia, which occurs in 15%[7] to 38%[8] of stroke patients and results in a reduction of communicative ability.

Numerous stroke studies have investigated the prevalence[9], course[2, 10], and predictive value[5, 11] of cognitive impairment after stroke. However, information on cognitive impairment in aphasic patients is limited. Most studies have explicitly excluded all patients with aphasia[9-10, 12] or those with severe aphasia[5, 13], because communication problems interfere with standard cognitive testing. Two studies have reported on the cognitive performance of aphasic patients[14-15], but the number of patients was small and not all cognitive domains were examined.

The aim of this observational prospective follow-up study was to investigate the prevalence and course of non-linguistic cognitive impairments in a large cohort of aphasic patients at 3 months and 1 year after stroke, and the association between aphasia, non-linguistic cognition, and functional outcome.

METHODS

Patients

Patients with aphasia due to a first-ever stroke were recruited from the stroke units of 17 hospitals in The Netherlands. They were screened by the local neurologist and speech-language therapist for the Sequential Prognostic Evaluation of Aphasia after stroKe (SPEAK) study from June 2007 to June 2009. Eligible patients were adult Dutch native/near-native speakers with an intracerebral hemorrhage or infarction who were testable with the ScreeLing[16-17] within 14 days after stroke. Included were patients with aphasia as confirmed by the speech-language therapist and in addition a score below the cut-off point of the Token Test (i.e. <29)[18] and/or the ScreeLing (i.e. <68)[17]. Patients with pre-stroke dementia (suspected or confirmed), psychiatric disorder, severe dysarthria, developmental dyslexia, severe perceptual disorders of vision and hearing, or illiteracy were excluded.

Patients and/or their close relatives gave written informed consent while admitted to hospital. The follow-up assessments were conducted in the subsequent setting, i.e. nursing home, rehabilitation center, or at home.

This study was approved by the medical ethics committees of Erasmus MC University Medical Center and of the participating centers.

Follow-up Assessments

Demographic data, collected at baseline, included age, sex, education level, and handedness. Neurologic data included stroke type, stroke localization, and stroke-related disability as measured by the Barthel Index[19], which is a 20-point scale to assess the degree of independence in general daily life activities (e.g. eating, getting dressed), and were also collected at baseline. At 3 months and at 1 year after stroke, non-linguistic cognitive abilities were examined within 4 domains:

(1) Abstract reasoning was assessed with Matrix Reasoning of the Wechsler Adult Intelligence Scale-III (WAIS-III)[20] and the visual Semantic Association Test[21], a modified version of the Pyramids and Palm Trees Test[22]; (2) Visual memory was measured with the direct and delayed recall of the visual reproduction test (Wechsler Memory Scale-III)[23], and the Short Recognition Memory Test for Faces from the Camden Memory Tests[24]; (3) Visual perception and construction was evaluated with the Bells Cancellation Test[20], Block Design (WAIS-III)[20], and the Clock Drawing Task[25-26]; (4) Executive functioning, i.e. selective, sustained, and divided attention, was assessed with the modified Wisconsin Card Sorting Test (WCST)[27], the Trail-Making Tests A, B (TMT A, B)[20], and the Weigl sorting test[28]. All the cognitive tests within each domain were selected to avoid oral output. The Mini-Mental State Examination (MMSE)[29] was used as a measure of global cognitive functioning.

The raw test scores were transformed into standardized scores (z-scores) based on the norms of each test. Specific norms adjusted for age, sex, and education level were used if available. Impairment was considered to be present when a patient's z-score was less than -2 on the corresponding test. Domain scores were calculated by averaging the z-scores of all tests belonging to the same cognitive domain. A cognitive domain was designated as impaired when at least 1 of the tests belonging to that cognitive domain was impaired.

Based on the number of impaired non-linguistic cognitive domains, patients were classified into 2 groups: severe cognitive impairment, i.e. ≥ 2 impaired cognitive domains out of 4, and mild cognitive impairment, i.e. < 2 impaired cognitive domains.

Language was assessed at 3 months and 1 year after stroke by means of:
1. The ScreeLing, designed to detect aphasia in acute stroke patients, and to reveal deficits in the 3 core linguistic components, i.e. semantics, phonology, and syntax (see appendix III).[16-17, 30] The ScreeLing correlates significantly with the Aphasia Severity Rating Scale (ASRS) of the Boston Diagnostic Aphasia Examination[31] and the Token Test[18], indicating good concurrent validity[17].
2. Spontaneous speech, elicited in a 10-minute semi-standardized interview on 4 topics, and evaluated with the ASRS of the Boston Diagnostic Aphasia Examination[31] as a measure of verbal communication (see appendix II).
3. The Token Test (TT), 36-items raw scores version, to measure the presence and the severity of aphasia.[18] Patients were classified into 2 groups: persisting aphasia, i.e. TT < 29, and recovered, i.e. TT ≥ 29. In addition, at baseline this test was used to describe initial aphasia severity ranging from 'very severe' to 'no aphasia'.[18]

For functional outcome we used the modified Rankin Scale (mRS), a measure of daily life functioning after stroke.[32] Poor functional outcome was defined as mRS 3-5 indicating functional dependence; good functional outcome as mRS 0-2 representing independence.[33]

Information on depression was monitored during the complete follow-up period by reviewing medical records and interviewing patients and often also their close relatives. Patients treated with anti-depressants were categorized as being depressed.

Statistical Analyses

First, we compared the non-linguistic cognitive domain scores of our cohort at 3 months and 1 year after stroke with norm scores, i.e. z-score = 0, by conducting one sample t tests. We compared the prevalence of non-linguistic cognitive domain impairments between the 2 time points using McNemar Tests, and the difference in the non-linguistic cognitive domain scores with paired t tests. To assess whether there was a difference in the ScreeLing, ASRS, and TT scores between the time points, ordinal and linear mixed models were used with Bonferroni correction since in the SPEAK study, 6 consecutive language assessments were conducted.[34] For this part of the study, we only report the language data at 3 months and 1 year after stroke.

Second, we compared patients with persisting aphasia with those who had recovered at both assessments. To compare the non-linguistic cognitive domain scores between these 2 groups we used independent t tests and the Mann-Whitney test. To assess whether this comparison was confounded by sex, age, or education level, we used independent t tests in different strata of sex, age (dichotomized as < 65 years and ≥ 65 years), and level of education (dichotomized as high, i.e. junior high school or middle vocational education up to university or low, i.e. unfinished elementary school up to sophomore high school or lower vocational education). We also compared functional outcome between patients with persisting aphasia and recovered patients for both assessments with the Mann-Whitney test.

Third, we compared cognitive impairment with respect to functional outcome with the Mann-Whitney test. Finally, for the prevalence of depression in the different subgroups of patients we conducted frequency analyses.

A value of $p < 0.05$ was considered statistically significant. All analyses were performed with SPSS 15.0 or R statistical software 2.7.

RESULTS

The baseline characteristics of the 147 included patients are shown in Table 1.

As measured by the Token Test at baseline, 28% of the patients had very severe, 22% severe, 26% moderate, 15% mild, and 9% had no aphasia. Of all patients, 30% had isolated aphasia, 60% had a leg paresis and/or arm paresis, and 27% had hemianopia in addition to aphasia.

We were able to assess 125 patients at 3 months (mean 92 days, SD 5.8) and 115 at 1 year (mean 372 days, SD 22) (Figure 1). A total of 35 out of 125 patients failed to perform or complete the TMT A, B, and the WCST at 3 months, and 27 out of 115 at 1 year.

All Patients

Compared with the norm scores, our cohort was impaired on the MMSE and on all non-linguistic cognitive domains. At 1 year, only the performance on visual perception and construction did not differ from the norm (Table 2).

Impairment of visual memory was most frequent, both at 3 months and 1 year. Impairment of visual perception and construction was least common. Only the prevalence of visual memory impairments decreased over time (Table 3). At 3 months

Table 1. Baseline Characteristics of the 147 Included Patients with Aphasia

Age, years, mean (SD)	67 (15)
Sex, *n (%)*	
Female	78 (53%)
Male	69 (47%)
Handedness, *n (%)*	
Right-handed	127 (86%)
Not right-handed (i.e. left or ambidextrous)	17 (12%)
Unknown	3 (2%)
Level of education, *n (%)*	
High[a]	73 (50%)
Low[b]	69 (47%)
Unknown	5 (3%)
Clinical localization of stroke, *n (%)*	
Left hemisphere	145 (99%)
Right hemisphere	2 (1%)
Stroke type, *n (%)*	
Cerebral infarction	126 (86%)
Intracerebral hemorrhage	21 (14%)
Barthel Index (0-20) at 4 days, median (interquartile range)	15 (7.75-20)

[a] Junior high school or middle vocational education up to university.
[b] Unfinished elementary school up to sophomore high school or lower vocational education.
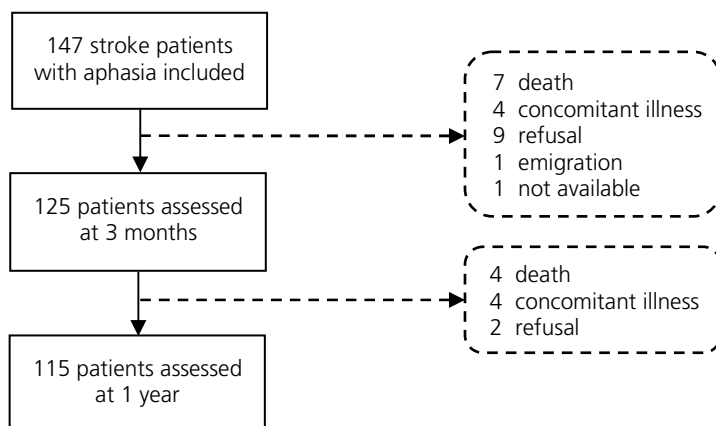

Figure 1. Flow Chart of the Included Patients

Table 2. Difference in Cognitive Scores between Cohort and the Norm (i.e. z = 0)

	3 months mean z-score (95 % CI)	1 year mean z-score (95 % CI)
Abstract reasoning	-0.96 (-1.24 to -0.67)	-0.89 (-1.21 to -0.58)
Visual memory	-2.05 (-2.27 to -1.83)	-1.80 (-2.03 to -1.56)
Visual perception and construction	-0.29 (-0.49 to -0.08)	-0.14 (-0.36 to 0.07)
Executive functioning	-0.76 (-0.92 to -0.60)	-0.60 (-0.75 to -0.45)
MMSE	-1.60 (-2.22 to -0.96)	-1.08 (-1.66 to -0.49)

CI, confidence interval; MMSE, Mini-Mental State Examination.

Table 3. Frequency of Cognitive Impairment and Comparison between the Assessments

	3 months	1 year	Improved	Deteriorated	p (McNemar)
Abstract reasoning	36 (32.1%)	30 (26.8%)	11 (9.8%)	5 (4.5%)	0.549
Visual memory	94 (83.2%)	88 (77.9%)	11 (9.7%)	5 (4.4%)	0.001
Visual perception and construction	21 (18.6%)	16 (14.2%)	9 (8.0%)	4 (3.5%)	0.754
Executive functioning	51 (46.4%)	39 (35.5%)	19 (17.3%)	7 (6.2%)	1.000
MMSE	30 (24.2%)	24 (21.1%)	9 (8.0%)	2 (1.8%)	0.065

MMSE, Mini-Mental State Examination.

107 (88%) patients were impaired in at least 1 non-linguistic cognitive domain. At 1 year this amounted to 91 patients (80%).

There was improvement between 3 months and 1 year on the MMSE and all non-linguistic cognitive domains, except for abstract reasoning. Of the scores on the language tasks, only the ASRS showed improvement (p < 0.003) (Table 4).

Patients with Persisting Aphasia versus Recovered Patients

At 3 months, 70 of the 125 patients assessed (56%) had recovered from aphasia, and at 1 year, 64 of the 115 patients (56%). At both assessments, the recovered patients had higher cognitive domain scores and MMSE scores than those with persisting aphasia (Table 5). This finding was independent of age, sex, and education level. Also, patients with persisting aphasia showed more impairment (i.e. impairments in ≥ 2 domains) than those who had recovered: at 3 months 75% versus 33% (p < 0.001); at 1 year 77% versus 23% (p < 0.001). Patients with persisting aphasia also more often had a poor functional outcome (mRS > 2) than the recovered patients: at 3 months 40% versus 15% (p = 0.002) and at 1 year 43% versus 13% (p < 0.001).

Patients with Non-Linguistic Cognitive Impairments and Depression

Patients with severe cognitive impairment more often had poor functional outcome than patients with mild cognitive impairment: 39% versus 9% (p < 0.001) at 3 months, and 43% versus 12% (p < 0.001) at 1 year.

Table 4. Comparison of Cognitive (Z-Scores) and Language (Raw Scores) Performance at 3 Months and 1 Year

	3 months (n=125)	1 year (n=115)	Mean Difference (95 % CI)
Cognitive assessment (mean z-scores)			
Abstract reasoning	-0.95	-0.85	0.10 (-0.08 to 0.29)
Visual memory	-2.00	-1.80	0.20 (0.09 to 0.31)
Visual perception and construction	-0.31	-0.09	0.21 (0.03 to 0.40)
Executive functioning[a]	-0.64	-0.43	0.21 (0.11 to 0.32)
MMSE	-1.67	-0.96	0.71 (0.28 to 1.14)
Language assessment (mean raw scores)			
ScreeLing total	61.76	63.27	1.51 (-0.90 to 3.92)
Semantics (maximum 24)	21.47	22.02	0.55 (-0.47 to 1.56)
Phonology (maximum 24)	19.57	20.20	0.63 (-0.37 to 1.63)
Syntax (maximum 24)	20.76	21.16	0.39 (-0.67 to 1.45)
Token Test (maximum 36)	26.51	26.84	0.33 (-3.14 to 3.80)
Aphasia Severity Rating Scale[b] (maximum 5)	4 (3-5)	5 (4-5)	

CI, confidence interval; MMSE, Mini-Mental State Examination.
Higher scores are associated with better performance.
[a] At 3 months the assessment of executive functioning was completed in 90 patients and at 1 year in 88.
[b] median (interquartile range).

Finally, depression occurred in 11% of the entire cohort: at 1 year more often in patients with persisting aphasia (20%) than in recovered patients (6%), and more often in patients with severe cognitive impairment (20%) than in those with mild cognitive impairment (5%).

DISCUSSION

Our study shows that non-linguistic cognitive impairments are common in patients with either persisting or recovered aphasia in the first year after stroke. Both at 3 months and at 1 year, visual memory was most frequently affected, and impairment in visual perception and construction least frequently. We found improvement on the MMSE, visual memory, visual perception and construction, and executive functioning. Of the language assessments, only the ASRS results improved between 3 months and 1 year. At both assessments, patients with persisting aphasia had lower cognitive domain scores and MMSE scores, and more severe cognitive impairment than patients who had recovered from aphasia. Patients with persisting aphasia also more often had a poor functional outcome and depression. Furthermore, poor functional outcome and depression were more frequent in patients with severe cognitive impairment than in those with mild cognitive impairment. These findings stress the importance of assessing non-linguistic cognition in patients with aphasia

Table 5. Comparison of Mean Cognitive Z-Scores of Patients with Persisting Aphasia (TT < 29) and Recovered Patients (TT ≥ 29)

	Persisting Aphasia	Recovered	Mean Difference[a] (95 % CI)
Abstract reasoning			
3 months	-1.68 (n=55)	-0.42 (n=70)	-1.26 (-1.85 to -0.67)
1 year	-1.62 (n=51)	-0.29 (n=64)	-1.34 (-2.00 to -0.67)
Visual memory			
3 months	-2.59 (n=55)	-1.62 (n=70)	-0.97 (-1.39 to -0.56)
1 year	-2.33 (n=51)	-1.39 (n=64)	-0.94 (-1.42 to -0.46)
Visual perception and construction			
3 months	-0.80 (n=55)	0.10 (n=70)	-0.90 (-1.34 to -0.46)
1 year	-0.78 (n=51)	0.32 (n=64)	-1.11 (-1.55 to -0.66)
Executive functioning			
3 months	-1.12 (n=27)	-0.61 (n=63)	-0.51 (-0.84 to -0.18)
1 year	-0.93 (n=27)	-0.44 (n=61)	-0.49 (-0.80 to -0.17)
MMSE			
3 months	-4.06 (n=55)	0.13 (n=70)	-4.20 (-5.52 to -2.87)
1 year	-2.89 (n=51)	0.34 (n=64)	-3.22 (-4.38 to -2.07)

TT, Token Test; CI, confidence interval; MMSE, Mini-Mental State Examination.
Higher scores are associated with better performance.
[a] Independent of age, sex, and education level.

due to stroke in addition to language assessment as cognitive impairment may influence their rehabilitation. Moreover, aphasic patients may also benefit from psychological treatment and/or medication since the prevalence of depression was higher in the patients with persisting aphasia than in those who recovered.

Strength of our study is that it is the first to assess non-linguistic cognitive impairments prospectively and thoroughly in a large cohort of patients with aphasia after stroke. Furthermore, this study is the first report on the difference in cognitive performance between patients with persisting aphasia and those who recovered. A limitation is that although we applied a non-linguistic cognitive test battery of well-known and well-validated tests suitable for patients with aphasia, we cannot rule out that patients used covert language as a tool to process non-linguistic tasks.[35] Another limitation is that we were unable to perform cognitive assessment in the acute stage, since it has been reported that acute cognitive impairments influence cognitive and functional outcome.[11] Half of our patients had severe aphasia in the acute stage which hampered early and extensive cognitive examination. This is probably the reason why most previous studies on cognitive outcome after stroke have excluded patients with aphasia, even when conducted in the post-acute stage.[9-10, 12] In this study, we were able to perform cognitive assessment in most patients using standard test instructions with

examples, since the severity of aphasia had diminished substantially at 3 months and 1 year; the performance on comprehension measures (semantics and TT) was quite well (Table 4). A test was not administered when a patient failed the example or, in case of no example, failed the first items because the instruction could not be comprehended. A further limitation is that we did not perform extensive neuropsychiatric assessments, particularly of mood disorders. We did, however, review medical records and performed interviews with all patients and often also with their relatives. Furthermore, our cognitive assessment included several aspects of a neuropsychiatric assessment (e.g. overall questions on mood, behavior etc.) to ascertain that the cognitive scores were not influenced by possible neuropsychiatric disorders. All patients who had depression in our study were already treated for this disorder.

Our data show that 56% of the patients who were assessed at 3 months after stroke had recovered from aphasia. This is in line with a previous study that reported that 44% of their patients had fully recovered from aphasia already at the time of discharge from the hospital.[8]

The reported prevalence of non-linguistic cognitive impairment at 3 months after stroke ranges from 17% to 68%,[5, 10, 12, 36] and at 1 year from 27% to 73%,[9, 37] which is much lower than in our study (88% and 80% respectively). This difference may be caused by the fact that most of these previous studies excluded patients with aphasia[12] or with severe aphasia[5]. An additional reason could be that some studies used only a cognitive screening tool and not an extensive cognitive assessment.[36]

Our finding that visual memory was most frequently impaired is consistent with an earlier study[5] using a similar task, i.e. the visual reproduction test[23]. It has been reported that aphasia is related to memory impairments.[38]

Impairments in visual perception and construction are reported to be primarily associated with right hemisphere lesions.[39] Therefore it was expected that impairments in this domain would be less frequent in our cohort since nearly all our patients had left hemisphere lesions. The prevalence of impairments in executive functioning and abstract reasoning are in line with an earlier study that examined the prevalence of impairments in various cognitive domains in the acute stage of stroke.[1] Finally, the prevalence of cognitive impairments as measured with the MMSE was lower than on the extensive cognitive test battery. This is consistent with the report that MMSE is moderately sensitive in screening for cognitive impairments, particularly in stroke patients, and that additional cognitive examination in patients with normal MMSE scores results in detecting more cognitive impairments.[40]

With respect to recovery, we found improvement in almost all non-linguistic cognitive domains which is in line with an earlier study that also reported improvement after 3 months.[2] In contrast, in the language domain, we only found improvement on the ASRS, a measure of verbal communication. On the other language tests, the recovery process had already reached a plateau within the first 3 months after stroke.[34] This is consistent with the general agreement that for the main part aphasia recovery occurs within the first couple of months after stroke.[8] The prolonged recovery of verbal communication suggests that non-linguistic cognitive functions, e.g. executive functioning, may be involved in verbal communication where the main language components (i.e. semantics, phonology, and syntax) are integrated.

Our finding that patients with persisting aphasia had lower cognitive scores, more severe cognitive impairment, and more often a poor functional outcome, is consistent with a previous study in which a small group of severe aphasics was compared with a group of mild or moderate aphasics.[14] Our result that patients with persisting aphasia had a higher prevalence of depression than patients who had recovered, is in line with the report that aphasic patients are more often depressed compared with stroke patients without aphasia.[14]

To summarize, non-linguistic cognitive impairments are common in patients with acute aphasia after stroke, at 3 months as well as at 1 year. Although improvement occurred in most non-linguistic cognitive domains and verbal communication, our cohort remained impaired. This implies that patients with aphasia may benefit from an extensive cognitive assessment in addition to language assessments in order to optimize the rehabilitation process.

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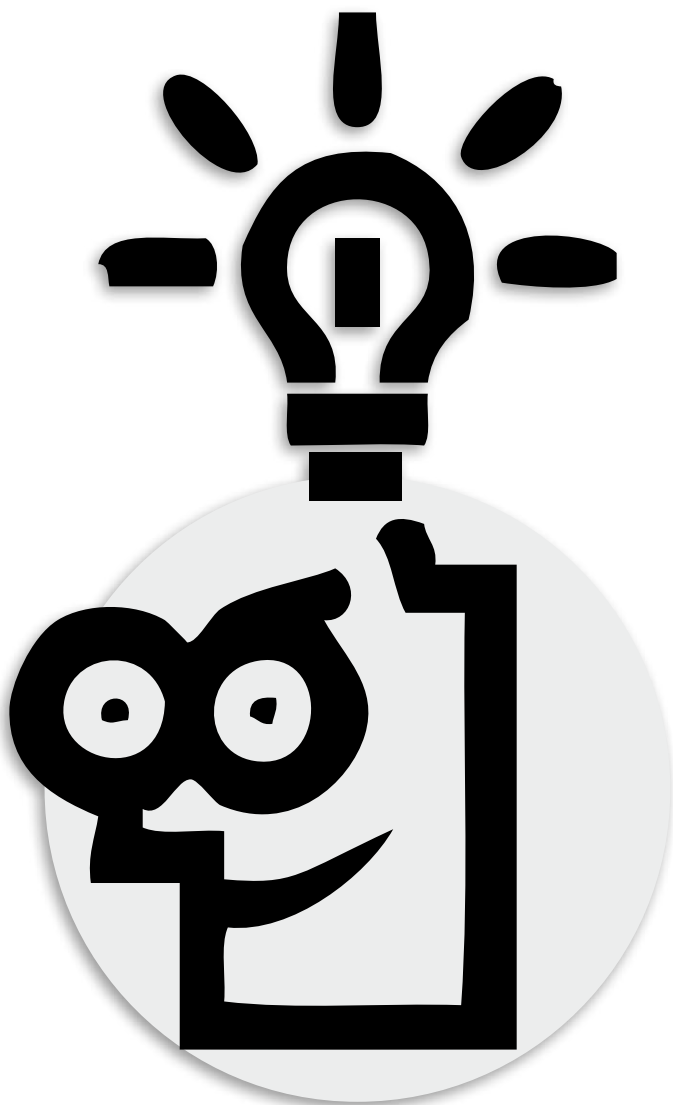
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GENERAL DISCUSSION

In this thesis, I investigated the course of aphasia during the first year after a first-ever stroke in a large cohort of patients. I have examined the occurrence, recovery, and prognostic value of deficits in semantic, phonological, and syntactic processing, which are the main linguistic components of communication. Furthermore, I have explored the prevalence and recovery of non-linguistic cognitive deficits, which are also common in stroke populations, and their relation with aphasia and outcome.

In this chapter, I will summarize the main findings of the conducted studies, discuss their methodological aspects, and their implications for clinical practice. Finally, I will provide some suggestions for future research.

MAIN FINDINGS

In order to be able to examine semantic, phonological, and syntactic deficits starting from the first few days after stroke, one needs a test that not only aims at detecting these deficits, but is also feasible in acute patients who are often unable to tolerate a lengthy aphasia test battery. Of the 8 screening tests that we have identified in our systematic review, the ScreeLing[1-2] proved to be the only test designed to assess deficits on the main 3 linguistic components in addition to being the most accurate and the most reliable in differentiating between stroke patients with and without aphasia.

We explored the feasibility and significance of investigating the 3 linguistic components individually using the ScreeLing in a pilot study with a 3-year follow-up. The results showed that assessing the recovery of the linguistic components separately was relevant, as the recovery curves of the 3 components were not identical.

The results of our study on the occurrence of linguistic deficits were consistent with an earlier study with a small sample size showing that selective linguistic deficits can already be detected early after stroke[1] and underlined the relevance of investigating the 3 components individually. We found that about 22% of the patients had a deficit in only 1 component, with phonology as the most frequently disturbed. Impairments of the 3 components had a different impact on verbal communication and the number of impaired linguistic components was related with the severity of aphasia.

In our prognostic study we found that phonology was the strongest predictor for the outcome of aphasia at 1 year after stroke. The best model for predicting aphasia outcome as early as the first week after stroke, consisted of the phonology score, the Barthel Index score, age, educational level, and stroke subtype. The addition of phonological recovery between 1 week and 6 weeks after stroke to this model increased the explained variance.

Our study of the recovery of the 3 linguistic components confirmed the results of our pilot study in which we showed that the recovery curves of semantic, phonological, and syntactic processing are not alike: phonological recovery continued the longest and was similar to the recovery on the Token Test[3], a measure of aphasia severity. The recovery of verbal communication persisted after the recovery of the linguistic components had already stabilized.

In patients with aphasia after stroke, non-linguistic cognitive deficits are common, even in the patients that recovered from aphasia. When comparing the recovered

patients with the ones with persisting aphasia, we found that the ones with persisting aphasia showed more non-linguistic cognitive impairments and more often had a poor functional outcome. We also found a higher prevalence of depression which is in line with a previous study[4] reporting on aphasic patients being more often depressed than patients without aphasia.

METHODOLOGICAL ASPECTS

It is not easy to conduct a thorough assessment of aphasia after stroke in a large-scale multicenter study like SPEAK. First, in the acute stage an extensive aphasia test battery is too much of a burden for the often ill patients. Second, we conducted repeated assessments during the 1 year follow-up which had to fit in the rehabilitation program of the patients as well as in their daily activities after finishing the rehabilitation phase. Third, in addition to investigating the aphasia symptoms, we wanted to investigate other factors in our cohort, such as functional outcome and non-linguistic cognitive deficits. We therefore had to limit the aphasia assessment in the acute as well as in the chronic stage, and we were forced to choose our selection of aphasia tests very carefully in order to measure language improvements. Our main goal was to gain insight into the deficits on the 3 main linguistic components for which only the ScreeLing[1-2] was suitable. Given that patients with aphasia and their family primarily complain about their inability to communicate adequately, leading to loneliness, isolation, and a failure to return to work, we chose verbal communication, evaluated by the Aphasia Severity Rating Scale (ASRS)[5], as our primary outcome measure. Since initial aphasia severity has been reported to be an important prognostic factor and to have a tendency to be associated with mortality[6], we decided to include the Token Test[3], a well-known and well-validated measure for aphasia severity. This compilation of aphasia tests alone took about 1 hour to complete in the acute stage. Hence, we could not add an extensive test battery such as the Aachener Aphasie Test[7] or tasks from the Psycholinguistic Assessments of Language Processing in Aphasia[8], which could have provided us with more detailed information about the nature of, for example, the phonological deficits with respect to prognosis.

Assembling a cognitive test battery that is suitable for patients with aphasia after stroke was one of the most difficult challenges we had to deal with. A standard test battery that is used in clinical practice to assess cognition is not appropriate for patients with aphasia, because of their language deficits. For example, a frequently used measure to assess memory is a Dutch adaptation of the Verbal Learning Test[9-10], the Groningen 15 words test. In this test, 5 trials of 15 monosyllabic words are presented subsequently. Immediately after each trial, patients have to recall as many words as possible. In addition, there is a delayed recall and a recognition trial. A patient with aphasia would anyhow be put at a disadvantage on this test, because of word finding deficits, without necessarily having memory impairment. Therefore, a cognitive test battery was needed that was not heavily dependent on language skills. The selected tests had to be standardized, validated, and available in the Netherlands. In order to avoid tests that are dependent on verbal output, we were bound to select tests that were dependent on non-verbal visual output. A disadvantage of this approach was that for patients with a hemiparesis some tests could be confronting

or lead to more frustration than for the patients without a hemiparesis, for example during the clock drawing test. We expected that at 3 months after stroke, when the cognitive test battery would be used for the first time, the patients with a hemiparesis would have learned to deal with the weakness of the preferred hand during their rehabilitation and used to using the non-preferred hand more often. Even though not ideal, we tried to minimize the number of tests in which patients are asked to make drawings. Another criterion was that the test battery should be suitable for patients with severe aphasia as well as for patients with mild aphasia, since at 3 months and at 1 year after stroke a large portion of the patients was expected to be completely recovered or considerably improved.[11-12] Therefore, we aimed at selecting tests with an increasing level of difficulty and with stop points, so that the test can be discontinued after a certain number of errors. Finally, we wanted to examine the different cognitive domains as thorough as possible within a maximum of 2 hours, since, as stated earlier, we wanted to investigate other variables as well and the assessment had to be fitted in the daily program of the patients. An extensive neuropsychiatric assessment was not possible due to limited assessment time.

Regarding our patient inclusion, there were large differences in the numbers of patients that were included in the participating hospitals. Perhaps, selection bias played a role in this variation. Another possibility is the difference in specialization of the participating hospitals in the different regions. For example, in 1 city 2 hospitals participated, with 1 including only 2 patients and the other 12. After asking the speech-language therapists about this difference, they explained that almost all stroke patients were referred to the hospital with the largest number of inclusions. The other hospital evaluates preferably patients with tumors and neurodegenerative disorders.

The choice of the main outcome measure in our prognostic study, i.e. verbal communication, might have influenced our results. In a previous prognostic study with a much smaller group of patients, the semantic component proved to be the strongest predictor and not phonology.[13] However, the outcome measure in that study was not verbal communication as in our study, but general functional communication which was measured with the Communication Activities of Daily Living (CADL)[14]. The CADL includes tasks that require a wide range of abilities such as the use of numbers, reading, writing, and nonverbal communication.

Common and unavoidable aspects of observational follow-up studies are missing data and the impossibility to draw conclusions on the effect of treatment. Compared with other studies our rate of missing data was small[15] and we gathered at least some information on the speech-language therapy in contrast to some other studies[15-16]. Another aspect of conducting this type of research is that there is usually only 1 cohort included that is large enough to answer the research questions. Our cohort was just large enough to be able to estimate the influence of 12 prognostic variables.[17] The validation of the prognostic model presented in this thesis should be considered in future studies with cohorts from other hospitals, regions, and countries.

Possibly, not all prognostic factors have been included in our regression model since about 40% of the variance in the outcome of aphasia at 1 year after stroke remained unexplained. Clearly, there are still factors out there that are not yet identified. We chose the independent variables on the basis of previous studies[6, 11, 16]

and a priori clinical judgment. No study on the prognosis of aphasia after stroke will ever manage to find an explained variance of 100%.

The results described in this thesis are limited to patients with aphasia after a first-ever stroke, since we excluded patients with aphasia after a recurrent stroke. It might be that the results differ in a cohort of patients with a recurrent stroke. However, in another study in which patients with a first-ever stroke as well as a recurrent stroke were included, having had a previous stroke was not related to aphasia recovery.[11]

The strong points of the SPEAK study are that it is the first study in which the course of the recovery of semantic, phonological, and syntactic deficits are examined, in addition to their prognostic value for the outcome of aphasia at 1 year after stroke. Furthermore, it is the first study in which the prevalence and course of non-linguistic cognitive deficits in patients with aphasia are investigated.

CLINICAL IMPLICATIONS

Across the several studies described in this thesis, one finding was particularly remarkable: the key role of phonology in the occurrence of selective deficits in aphasia, in the prognosis, and in the recovery of aphasia after stroke. What do these findings imply? Should researchers concentrate on testing different aspects of phonological processing and developing specific treatment programs for phonological deficits? Unfortunately, as I stated earlier, it is impossible to answer questions about treatment on the basis of 1 or more studies. In the latest report from the Cochrane Stroke Group in which 30 aphasia therapy studies were critically reviewed, it was suggested that patients with aphasia after stroke may benefit from speech-language therapy, but there was insufficient evidence to indicate the best approach to delivering speech-language therapy.[18] This conclusion was consistent with a recent randomized controlled trial that found no difference in efficacy between cognitive linguistic therapy and communicative therapy.[19] Based on our results we can only recommend to examine the phonological component thoroughly during the first 3 months after stroke, and especially in the first 6 weeks in which the recovery of phonological deficits adds to the prognostic value of our model.

Another finding, important but perhaps less remarkable for those with clinical experience as speech-language therapists, is that non-linguistic cognitive impairments are common in patients with aphasia after stroke. Our results confirm earlier reports on stroke patients without aphasia that cognitive impairment is associated with poor recovery[20] and poor functional outcome[21], and interferes with the rehabilitation process. Therefore, we recommend assessing non-linguistic cognitive functioning in all patients with aphasia in addition to depression starting from 3 months after stroke.

FUTURE RESEARCH

The studies in this thesis have generated several research questions which should be investigated in future studies.

Our finding that, of the 3 linguistic components, phonology proved to be the strongest predictor for verbal communication at 1 year after stroke might be related to differences in lateralization. In a recent meta-analysis it has been reported that

semantic and syntactic processing activates the right as well as the left hemisphere, while phonological processing is more unilaterally localized in the left hemisphere.[22] Possibly this could explain the important role of phonology in our study, since our cohort almost entirely consists of patients with left-hemisphere lesions. fMRI studies try and aim to localize the brain areas that are specific for semantic, phonological, and syntactic processing. The same type of studies could be used to gain more insight into the underlying neural mechanisms of the recovery of the 3 linguistic components. Currently in FIAT (Functional Imaging in Aphasia Treatment), we investigate the neural mechanisms of the effect of semantic and phonologic treatment on verbal communication.

Future studies on the prognosis of aphasia after stroke are necessary to validate our prognostic model. The focus should be on a more thorough examination of the phonological component which could result in more detailed information on the prognostic relevance of the specific nature of the phonological deficit. Data on each of the 4 phonological tasks are currently being analyzed.

Aphasia therapy studies should aim at investigating whether phonologically based treatment improves outcome, whether it is better to provide treatment on the basis of the affected linguistic component, and whether it should be started during the recovery period of 3 months after stroke, or after the recovery process has stabilized. In a current randomized controlled trial, RATS-3 (Rotterdam Aphasia Therapy Study), we study the effect of a short period of intensive semantic and phonological therapy started early after stroke compared with the effect of delayed therapy.

It is already known that the quality of life in patients with aphasia after stroke is reduced. However, the exact impact of the different linguistic components has not been investigated as well as the evolution of quality of life during the first year after stroke. Data from SPEAK are available and will be analyzed to answer these questions.

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x o y p g r a i g
u a r r e e m o p
y o t h o p q a u
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9

SUMMARY / SAMENVATTING

SUMMARY

This thesis describes and analyses the recovery and prognosis of aphasia during the first year after stroke onset. Patients with a first-ever stroke were recruited from stroke units of various participating hospitals in the Netherlands. The occurrence, recovery, and prognostic value of semantic, phonological, and syntactic deficits were examined as well as the prevalence and recovery of non-linguistic cognitive deficits, and their relation with aphasia and functional outcome.

In the general introduction, ***Chapter 1***, the background and objective for the research described in this thesis are presented.

In ***Chapter 2***, a systematic review of the literature to identify available screening tests for differentiation between patients with and without aphasia after stroke is described. Eight screening tests were selected and evaluated in terms of accuracy, reliability, and feasibility. Four of the identified tests were rated as having a 'low risk of bias' of which the ScreeLing was the most accurate and most reliable. Future research should focus on a better validation of the available aphasia screening tests in stroke patients, using validation methods that minimize the risk of bias.

Chapter 3 focuses on a pilot study that explored the importance of examining the recovery curves of semantic, phonological, and syntactic processing. Fifteen patients were assessed at 6 time points during a 3-year follow-up. We found that the recovery curves of the 3 linguistic components were not the same, indicating that it is meaningful to investigate the recovery of the 3 components separately.

Chapter 4 reports the psychometric properties of the ScreeLing and the occurrence of linguistic deficits at 12 days after stroke onset. In addition, the relationship between these linguistic deficits and overall aphasia severity as well as the quality of verbal communication was examined. The ScreeLing was found to be a valid and reliable test for assessing deficits in semantic, phonological, and syntactic processing in patients with aphasia after stroke. Deficits in only 1 of the 3 linguistic components were found in 22.4% of the patients, with the phonological component as most frequently defected. The more linguistic components were impaired, the more severe was the aphasia. Phonology was most related with verbal communication.

In ***Chapter 5***, we present the results of our prognostic study in which we investigated the prognostic value of linguistic, demographic, and clinical stroke characteristics with respect to the outcome of aphasia at 1 year. The phonology score, the Barthel Index score, age, education level, and stroke subtype in the first week after stroke, appeared to be good predictors of the verbal outcome of aphasia at 1 year after stroke. Of all significant predictors, phonology was the strongest. Adding the degree of recovery of phonological processing within the first 6 weeks to the baseline model, improved its prognostic value.

Chapter 6 describes a 1-year follow-up study on the recovery of deficits in semantic, phonological, and syntactic processing in 147 patients with aphasia after a first-ever stroke. The recovery of verbal communication and of aphasia severity were also investigated. We conducted 6 assessments and found that the linguistic components do not improve simultaneously: semantic and syntactic processing improved up to 6 weeks; phonological processing up to 3 months, just as aphasia

severity (i.e. Token Test). Verbal communication (i.e. ASRS) improved up to 6 months after stroke.

In *Chapter 7*, we report on the prevalence and course of non-linguistic cognitive impairments in patients with aphasia after stroke, and their association with aphasia and functional outcome. The majority of the patients had impairments in at least 1 cognitive domain at both 3 months and 1 year. Visual memory was most frequently affected and visual perception and construction the least. Improvement on the MMSE and all cognitive domains was observed, except for abstract reasoning. Patients with persisting aphasia had lower non-linguistic cognitive domain scores, worse functional outcome, and were more often depressed than those who had recovered from aphasia. We recommend standard non-linguistic cognitive assessment in patients with aphasia after stroke.

The general discussion in *Chapter 8* summarizes the main findings of the studies presented in this thesis, elaborates on their methodological aspects, and reflects on their clinical implications. Finally, suggestions for future research are made.

SAMENVATTING

Dit proefschrift is gericht op het onderzoeken van het herstel en de prognose van afasie gedurende het eerste jaar na de beroerte. Patiënten met een eerste beroerte in de stroke-units van verschillende deelnemende ziekenhuizen in Nederland werden geïncludeerd. Het voorkomen, het herstel en de prognostische waarde van semantische, fonologische en syntactische stoornissen werd onderzocht, evenals de prevalentie en het herstel van 'niet-talige' cognitieve stoornissen. Ook is gekeken naar de relatie van 'niet-talige' cognitieve stoornissen met afasie en met de functionele uitkomst.

De inleiding, **Hoofdstuk 1**, geeft de achtergrond en de doelstelling weer van de studies die in dit proefschrift beschreven zijn.

In **Hoofdstuk 2** wordt een systematisch literatuuronderzoek gerapporteerd, verricht om beschikbare screeningstests te identificeren voor het onderscheiden van patiënten met en zonder afasie na een beroerte. Acht screeningstests zijn geselecteerd en geëvalueerd in termen van accuraatheid, betrouwbaarheid en uitvoerbaarheid. Vier van de tests werden gewaardeerd als een 'laag risico op bias' waarvan de ScreeLing het meest accuraat en meest betrouwbaar was. Toekomstig onderzoek zou zich moeten richten op een betere validatie van de beschikbare afasie screeningstests bij patiënten met een beroerte via een methode die het risico op bias minimaliseert.

Hoofdstuk 3 omvat een proefonderzoek waarin het belang werd verkend van het onderzoeken van het herstel van de semantische, fonologische en syntactische verwerking afzonderlijk. Vijftien patiënten zijn 6 keer onderzocht in een follow-up van 3 jaar. Het bleek dat de herstelcurves van de 3 linguïstische componenten niet hetzelfde waren, hetgeen het belang aangaf van het onderzoeken van het herstel van de 3 componenten afzonderlijk.

Hoofdstuk 4 geeft de psychometrische aspecten van de ScreeLing weer en het voorkomen van linguïstische stoornissen op 12 dagen na de beroerte. Het voorkomen van deze linguïstische stoornissen werd gerelateerd met de ernst van de afasie en met de kwaliteit van de verbale communicatie. De ScreeLing bleek een valide en betrouwbare test te zijn voor het meten van stoornissen in de semantische, fonologische en syntactische verwerking bij patiënten met een afasie tengevolge van een beroerte. Bij 22.4% van de patiënten werd slechts een stoornis gevonden van 1 component, waarbij stoornissen van de fonologische component het meest frequent voorkwamen. Hoe meer linguïstische componenten gestoord waren, des te ernstiger was de afasie. Fonologie was het meest gerelateerd aan verbale communicatie.

In **Hoofdstuk 5** worden de resultaten van ons prognostisch onderzoek gepresenteerd waarin de prognostische waarde van linguïstische, demografische en klinische stroke karakteristieken onderzocht werd in relatie tot de uitkomst van de afasie op 1 jaar na de beroerte. De fonologie score, Barthel Index score, leeftijd, opleidingsniveau en het subtype van de beroerte in de eerste week, bleken goede voorspellers van de kwaliteit van de verbale communicatie op 1 jaar. Van alle significante voorspellers was fonologie het meest robuust. Het toevoegen van de mate van het fonologische herstel binnen de eerste 6 weken aan het baseline model, verbeterde de prognostische waarde.
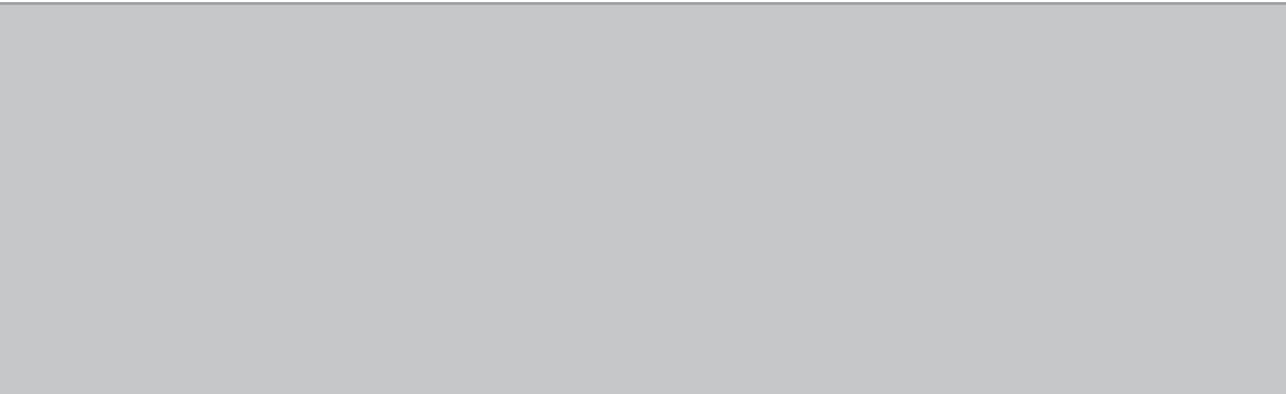
Hoofdstuk 6 is een beschrijving van een 1-jarig vervolgonderzoek naar het herstel van stoornissen in de semantische, fonologische en syntactische verwerking bij 147 patiënten met een afasie na een eerste beroerte. Het herstel van de verbale communicatie (ASRS) en van de ernst van afasie (Token Test), zijn ook onderzocht. We hebben 6 testonderzoeken uitgevoerd en vonden dat de linguïstische componenten geen simultaan herstel volgden: de semantische en syntactische verwerking ging tot en met 6 weken vooruit en de fonologische verwerking tot en met 3 maanden, parallel met de ernst van de afasie. De verbale communicatie ging tot en met 6 maanden na de beroerte vooruit.

In *Hoofdstuk 7* rapporteren we over de prevalentie en het verloop van 'niet-talige' cognitieve stoornissen bij patiënten met een afasie na een beroerte en over de associatie van deze stoornissen met afasie en de functionele uitkomst. De meerderheid van de patiënten had op zowel 3 maanden als 1 jaar stoornissen in minstens 1 cognitief domein. Het visuele geheugen was het meest frequent aangedaan en de visuele perceptie en constructie het minst. Er was vooruitgang op de MMSE en alle cognitieve domeinen, met uitzondering van abstract redeneren. Patiënten met een blijvende afasie hadden lagere 'niet-talige' cognitieve domeinscores, een slechtere functionele uitkomst en waren vaker depressief dan diegenen die van de afasie hersteld waren. Een standaard 'niet-talig' cognitief onderzoek bij patiënten met afasie na een beroerte wordt aanbevolen.

De discussie in *Hoofdstuk 8* vat de belangrijkste bevindingen van de onderzoeken die in dit proefschrift gepresenteerd zijn samen, bespreekt de methodologische aspecten van de onderzoeken en reflecteert over de klinische implicaties. Tot slot worden suggesties gedaan voor toekomstig onderzoek.

LIST OF ABBREVIATIONS

ANELT	Amsterdam-Nijmegen-Everyday-Language-Test
ASRS	Aphasia Severity Rating Scale
AUC	area under the receiver operating characteristic curve
BASA	Boston Assessment of Severe Aphasia
BDAE	Boston Diagnostic Aphasia Examination
CI	confidence interval
DOR	diagnostic odds ratio
EHI	Edinburgh Handedness Inventory
exp	expert assessment
FAST	Frenchay Aphasia Screening Test
FCP	Functional Communication Profile
LAST	Language Screening Test
LR+	likelihood ratio of a positive test
LR-	likelihood ratio of a negative test
MAST	Mississippi Aphasia Screening Test
MMSE	Mini-Mental State Examination
n.a.	not applicable
NCCEA	Neurosensory Center Comprehensive Examination for Aphasia
ne	neurologist
n.f.s.	not further specified
NGA	Norsk Grunntest for Afasi
n.r	not reported
nu	nurse
OR	odds ratio
PICA	Porch Index of Communicative Ability
ref	reference
ROC	receiver operating characteristic
SD	standard deviation
SE	standard error
SLT	speech-language therapist
SQ	Speech Questionnaire
SR	sentence repetition
sS	short Schuell
SSS	Scandinavian Stroke Scale
SST	Sheffield Screening Test for Acquired Language Disorders
STAND	Screening Test for Aphasia and Neurologic-Communication Disorders
SVF	Semantic Verbal Fluency
TT	Token Test
UAS	Ullevaal Aphasia Screening Test
VN	visual naming
WAB	Western Aphasia Battery
WF	word fluency

i e h o l r e l i a b i
n y a u t c p o x k c y
a g s t i h y r q b w o
o o i c c r c y e r i f
n l a o e o h c r v x n
i o y m n n n w e d a i
a n k e t i z t o q s l
t o i a e c s g k q g a
n h x b r t a h c x t r
w p w v r c v g a i i i
x p o o u t e r o t a e
n k k t o h p n o s c i
m e e c n o i t a c i n

l i t y o t h o p q a u
b n v g e a n a m t w h
f a n a b n i y i e e g
g o c i l r x e s m m n
s n l s m i n q o n f i
f i i e i t d r w i s n
t a n t c s r i d k e e
e t r c i h o p t h a e
f n l c a o u n h y k r
s w c g t i n j g g x c
s x e e f i c p m a v s
t n a m e s o s f a i b
u m m o c j t n t y n d

APPENDIX I: SEARCH STRING SYSTEMATIC REVIEW

The following search string was used for NLM PubMed-Medline and was adapted for the other databases:

(cerebrovascular disorders[mesh:noexp] OR brain ischemia[mesh] OR intracranial embolism and thrombosis[mesh] OR intracranial hemorrhages[mesh] OR stroke[mesh:noexp] OR vertebral artery dissection[mesh:noexp] OR stroke*[tw] OR poststroke*[tw] OR cva[tw] OR cvas[tw] OR cerebrovasc*[tw] OR cerebral vasc*[tw] OR ((cerebr*[tw] OR intracerebr*[tw] OR cerebell*[tw] OR brain*[tw] OR vertebrobasilar*[tw] OR intracran*[tw]) AND (infarct*[tw] OR ischem*[tw] OR ischaem*[tw] OR hemorrh*[tw] OR haemorrh*[tw] OR hematom*[tw] OR haematom*[tw] OR thrombos*[tw] OR thrombot*[tw] OR thromboembol*[tw] OR thrombol*[tw] OR apoplex*[tw] OR emboli*[tw] OR bleed*[tw]))) AND (aphas*[tw] OR logastheni*[tw] OR logagnos*[tw] OR logamnes*[tw] OR alogi*[tw] OR anepia*[tw] OR dysphasi*[tw] OR lichtheim*[tw]) AND (test[tw] OR tests[tw] OR testing*[tw] OR screen*[tw] OR tool*[tw] OR instrument*[tw] OR assessment*[tw]) AND (accura*[tw] OR sensitiv*[tw] OR specificit*[tw] OR psychometr*[tw] OR psycho-metr*[tw] OR predictive value*[tw])

APPENDIX II: APHASIA SEVERITY RATING SCALE

0. No usable speech or auditory comprehension.

1. All communication is through fragmentary expression; great need for inference, questioning, and guessing by listener. The range of information that can be exchanged is limited, and the listener carries the burden of communication.

2. Conversation about familiar subjects is possible with help from the listener. There are frequent failures to convey the idea, but the patient shares the burden of communication.

3. The patient can discuss almost all everyday problems with little or no assistance. Reduction of speech and/or comprehension, however, makes conversation about certain material difficult or impossible.

4. Some obvious loss of fluency in speech or facility of comprehension, without significant limitation on ideas expressed or form expression.

5. Minimal discernible speech handicap; the patient may have subjective difficulties that are not obvious to the listener.

Goodglass H, Kaplan E, Barresi B. *Boston diagnostic aphasia examination-third edition short form record booklet*. Austin, Texas: PRO-ED, Inc; 2001.

APPENDIX III: SCREELING

The ScreeLing is developed as a simple clinical aid in the first screening of disorders of the linguistic components in aphasia and in making an appropriate referral to a speech-language therapist. The following requirements are met: short (30 minutes); suitable for bedside administration (1 booklet and a score sheet) by various disciplines; vivid material (color photographs, varying tasks); simple scoring system (right/ wrong). The test consist of 3 linguistic components with each 4 different tasks:

Semantics (24 items)

1. Word-picture matching (6 items); 6 photos of objects, 5 semantically related foils. A traditional task for semantic processing. Choosing out of semantically related objects requires more of semantic processing than a choice out of unrelated objects.[1]
   Example: *gorilla,* tiger, elephant, polar bear, wolf, giraffe.
2. Identifying semantically anomalous sentences (6 items); choice correct/incorrect. This task requires recognizing the violation of semantic selection restrictions. The meaning of a word has to be processed in relation to its context.[2]
   Example: 'The ice chose the wrong direction'.
3. Verbal semantic association (6 items); choice out of 4 words, i.e. 1 correct, 2 distracters semantically related with the target word, and 1 unrelated distracter. Differentiating between relevant and irrelevant semantic features of a word depending on the required association is necessary.[3-4]
   Example: letter: chalk, paint, *pen*, grass.
4. Odd-word out (6 items); choice out of 4. The word that does not fit into the same semantic category as the other 3 words has to be selected.[5]
   Example: violin, *siren*, trumpet, piano.

Phonology (24 items)

1. Repetition of words and phrases (6 items); a traditional task for examining phonological disorders in the output route. Phonological complexity is varied according to word length, consonant clusters, identical vowels, phoneme-grapheme correspondence.[6]
   Example: 'monopolie' (monopoly); 'de excentrieke antiekhandelaar' (the eccentric antique dealer).
2. Reading aloud words and phrases (6 items); the level of complexity matches the repetition task. Phonological processing may vary depending on the input route.[7]
   Example: 'macaroni' (macaroni), and 'de enthousiaste beroepsgoochelaar' (the enthusiastic professional magician).
3. Equal/unequal judgment of spoken word pairs (6 items); phoneme discrimination, choice yes/no. A well-known task to examine the phonological input route.[7]
   Example: 'straat-staart' (street-tail).
4. Matching first phoneme of a spoken word with the grapheme (6 items); choice out of 3. Phoneme analysis and phoneme-grapheme conversion is required.[7]
   Example: 'boek' (book): g, k, *b*.

Syntax (24 items)

1. Sentence-picture matching (8 items); choice out of 3 or 4 photographs. The task requires syntactic comprehension, including reversible sentences, subject-verb agreement, reflexive verbs, passive sentences, prepositions, and verb tense.[8]

    Example: sentence 'The man's hair is being cut by the woman'; 3 pictures (*i*) 'the man's hair is being cut by the man', (*ii*) 'the woman's hair is being cut by the man', (*iii*) *'the man's hair is being cut by the woman'*.

2. Wh-questions (4 items); a photographed situation with a 'Wh'-question. 'Wh'-questions require syntactic processing of the non-canonical sentence construction.[8-9]

    Example: 'Wie ziet dat hij een taartje pakt?' (Literally: 'Who sees that he a cake takes?') The photograph depicts a man and woman talking, while a boy takes a cake. The woman is looking at the boy.

3. Identifying syntactic incorrect sentences (6 items); choice correct/incorrect. This task requires processing of word order, subject-verb agreement, auxiliaries, and conjunctions.[8]

    Example: 'Die bloemen is veel te duur' (Those flowers is far too expensive).

4. Sentence completion with function words (6 items); choice out of 4 words or phrases. Foils are well-known for addressing syntactic processing: personal pronouns, arguments, prepositions, auxiliaries, and different forms of verb tense or transitive/intransitive verbs.[10]

    Example: 'De jongen geeft zijn vriendin….' (The boy gives his girlfriend...) naar de film (to the movie), *parfum (perfume)*, wandelen (hiking), van de chauffeur (of the driver).

For semantics and syntax all items are presented aurally as well as visually in order to get insight into the underlying linguistic disorder independently of the input route.

This is a description of the final version of the ScreeLing, referred to in chapter 4 to 7. In an earlier research version, all subtasks were validated against the judgment of a linguist.[11]

In this final version, the following phonologic and syntactic subtasks have been adapted. Phonology 3 and 4 consisted of respectively 'reverse the word' ('pan' → 'nap') and lexical decision ('cimputer'). Both tasks were replaced after item analyses. Phonology 3 appeared to relate to a general capacity to perform the required action rather than to intactness of phonological processing. The lexical decision task was too easy; 80% of the patients performed perfectly.

To reduce chance level in Syntax 1, more foils were added to the original choice of 2. Syntax 3, the selection of a grammatically correct sentence out of 3 possibilities, appeared to be too time-consuming for the acute stage. Syntax 4, repetition of sentences with mainly function words ('Deze zijn beter dan die daar' (These are better than those ones)), was replaced by an easier-to-score task; this ensures that the test can also be used by professionals from other disciplines, such as neurologists and neuropsychologists.

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Ayşe, je kan nu eindelijk tegen Ollie zeggen dat ik echt klaar ben! We hebben elkaar de afgelopen jaren wat minder gezien door allerlei omstandigheden, maar onze vriendschap is tegen alles bestand. De keren dat we elkaar weer zien, is het als vanouds en zo'n band is zeldzaam. Het is heel fijn te weten dat nu voor ons beiden rustigere tijden aangebroken zijn. Ik kijk ernaar uit weer samen te gaan shoppen of gewoon zoals 'the old day's' loempia's te gaan eten in de stad. We pakken de draad weer op waar we de vorige keer gebleven zijn!

Access, Excel, Teleform, SPSS, de KISS-methode, koffie, StatTransfer, snip………en ga zo maar door, allemaal zaken die ik of van jou geleerd heb of beter mee heb leren werken dankzij jou Krzysz. Je bent al sinds mijn studententijd bezig me wegwijs te maken in de wereld van de technologie en het leerproces is nog steeds niet over. Onlangs nog heb je me geleerd hoe ik van een figuur met 96 dpi, een figuur met 300 dpi kon maken. Vooral dit laatste weetje is tegenwoordig onmisbaar als je een artikel indient, de indiening wordt simpelweg ongedaan gemaakt. Je hebt de SPEAK formulieren gemaakt, de testmoment-syntax waardoor ik door het invoeren van een ziektedatum van een patiënt een overzicht van alle testdata kreeg voor de rest van de follow-up en noem maar op. Kortom je hebt de logistiek van SPEAK een stuk simpeler en behapbaar gemaakt. Tijdens de momenten dat mijn stresslevel echt de pan uitrees wist je me door je nuchtere houding en KISS-methode meteen tot bedaren te brengen. Je bent gedurende de afgelopen jaren een ware vriend geworden die altijd voor me klaar staat en niet alleen tijdens de 112-momenten. Wetende dat ik altijd op jou kan rekenen was de beslissing om je ook voor deze belangrijke dag te vragen me bij te staan vanzelfsprekend.

Mijn familie wil ik bedanken voor de steun en ontspanning. Kleine man, door jou moest ik regelmatig noodgedwongen een pauze inlassen om samen met jou met Ernie te spelen. Je hield simpelweg niet op met vragen wanneer ik nou precies klaar zou zijn. Jouw bezoekjes waren vaak ook een extra stimulans om door te werken, zodat ik tijd overhield voor allerlei spelletjes. Loentje, dankzij alle puzzels die we samen in het puzzelboek hebben gemaakt ben ik op het idee gekomen voor de voorkant van mijn boek. Ik zal snel een nieuw puzzelboek kopen, zodat we weer samen kunnen zoeken naar woorden en verschillen. Noortjes, je wist inhoudelijk niet goed wat je aan het doen was, behalve dan gegevens controleren, maar jouw werk heeft tot hoofdstuk 4 geleid van dit proefschrift. Ik moest binnen enkele weken van 147 patiënten gegevens scannen, verifiëren, analyseklaar maken en vervolgens ook meteen analyseren en interpreteren. Jij hebt ervoor gezorgd dat ik de deadline heb gehaald, ontzettend bedankt! Hamid, Foeed en Hafida, we hebben alle 4 een zeer druk leventje en komen altijd tijd te kort. Als puntje bij paaltje komt staan we wel altijd voor elkaar klaar en laten we onmiddellijk alles uit onze handen vallen om elkaar te helpen. Dat is waar het om draait bij familie. Hamid, jij zorgde er onder andere voor dat mijn eerste 2 computers zo lang mogelijk probleemloos bleven draaien. Foeed, ik bleef fit en vitaal doordat ik kosteloos bij je mocht komen sporten. Hafida, je leest aan mijn tandvlees af hoe het met mij gesteld is. Hoe meer stress, des te slechter mijn mondgezondheid. Je wist voor de broodnodige ontspanning te zorgen door de vele bezoekjes naar de hammam, gezellige etentjes, winkel sessies, met als hoogtepunt de onvergetelijke vakantie naar Dubai. Ik kijk ernaar uit weer samen erheen te gaan! Raad, al van kleins af aan keek ik naar je op en wilde ik zijn zoals jij. Een hardwerkende, onafhankelijke vrouw met een groot hart, die ongelofelijk veel heeft bereikt in haar leven. Ik denk dat je je er niet bewust van bent, maar het feit dat ik zover gekomen ben is ook mede dankzij jou, bedankt voor alles.

Tot slot mijn lieve ouders die me altijd alles hebben gegeven wat mijn hartje begeert en ervoor gezorgd hebben dat ik niets te kort kwam. Jullie hebben me op alle mogelijke manieren geholpen en me er steeds op gewezen dat onderwijs geen plicht is, maar een groot recht. Vader, van het ophalen en brengen naar het station, tot het sjouwen van zware testtassen, tot het zorgen voor het jaarlijkse onderhoud van mijn auto, het plakken van stickers op testmapjes, proefpersoon zijn, tot………. Hnina, jouw wijze raad, geduld, zorgzaamheid, motiverende peptalks, en zo kan ik eindeloos doorgaan, waren echt onmisbaar. Woorden schieten te kort om te beschrijven wat jullie voor mij betekenen: hartelijk bedankt voor jullie onvoorwaardelijke steun en liefde.

ABOUT THE AUTHOR

Hanane El Hachioui was born on June 24th, 1982 in Rotterdam, the Netherlands. She attended secondary school at the O.S.G. Wolfert van Borselen in Rotterdam (VWO), where she graduated in 2000. The same year she started her training in psychology at Leiden University, with Clinical and Health Psychology as major, and Neuropsychology as specialization. During her psychology training she worked as a supervising assistant at the inpatients' clinic of the department of neuropsychiatry at Bavo Europoort. After obtaining her degree in psychology in 2005, she stayed at Leiden University as a fellow researcher at the department of Clinical and Health Psychology. She received a Mozaïek research grant from the Netherlands Organization for Scientific Research (NWO), and started in December 2005 the research described in this thesis at the department of Neurology at Erasmus University Medical Center under supervision of professor Peter J. Koudstaal and professor Diederik W.J. Dippel. In 2011, she started a new project at Rijndam Rehabilitation Center on adapting the ScreeLing for foreign speakers with aphasia, while continuing her work on her PhD-thesis. At present, she is a member of the PhD-day organizing committee 2012 and works on a new project at the Department of Neurology aimed at the development of a bedside aphasia screening tool to be used by neurologists.

LIST OF PUBLICATIONS

El Hachioui H, Verschuur M, van de Sandt-Koenderman M, Dippel D, Koudstaal P, Visch-Brink E. Recovery of linguistic deficits in stroke patients: A three-year-follow up. *Brain and Language*. 2005;95:213-214. (abstract)

El Hachioui H. Prognose en kwaliteit van leven bij patiënten met een afasie: een prospectieve vervolg studie. (SPEAK: Sequential Prognostic Evaluation of Aphasia after stroKe). *Afasiologie*. 2006;28:62-62.

Visch-Brink EG, van de Sandt-Koenderman WME, **El Hachioui H**. *Screeling*. Houten: Bohn Stafleu van Loghum; 2010.

El Hachioui H, Lingsma H, Van de Sandt-Koenderman M, Dippel D, Koudstaal P, Visch-Brink E. Phonology is the strongest language component in predicting aphasia outcome after stroke. *Procedia - Social and Behavioral Sciences*. 2011;23:162-163. (abstract)

El Hachioui H, van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. A 3-year evolution of linguistic disorders in aphasia after stroke. *International Journal of Rehabilitation Research*. 2011;34:215-221.

El Hachioui H, Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. The Screeling: Occurrence of linguistic deficits in acute aphasia post-stroke. *Journal of Rehabilitation Medicine*. 2012;44:429-435.

El Hachioui H, Lingsma H, Van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. SPEAK, Sequential Prognostic Evaluation of Aphasia after stroke: Prognosis and Recovery. *Stem-, Spraak- en Taalpathologie*. 2012;17:95-97. (abstract)

El Hachioui H, Lingsma H, Van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. Recovery of aphasia after stroke: A one-year follow-up study. *Journal of Neurology*. 2012. 10.1007/s00415-012-6607-2.

El Hachioui H, de Jong-Hagelstein M. Het neurolinguïstisch huwelijk. In: Robert E, Visch-Brink EG, Beeckman AS, eds. *Het (voor)beeldig brein: Taal & interventionele geneeskunde.* Antwerpen-Apeldoorn: Garant; 2012: *in press*.

El Hachioui H, Lingsma H, Van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. Long-term prognosis of aphasia after stroke. *Journal of Neurology, Neurosurgery and Psychiatry. Accepted.*

El Hachioui H, Lingsma H, Van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. Non-linguistic cognitive impairments in post-stroke aphasia: A prospective study. *Neurorehabilitation and Neural Repair. Major revision.*

El Hachioui H, Van de Sandt-Koenderman MW, Dippel DW, Koudstaal PJ, Visch-Brink EG. Screening tests for aphasia in patients with stroke: A systematic review. *Submitted.*

PHD PORTFOLIO

Name PhD student: Hanane El Hachioui
Erasmus MC Department: Neurology
Research School: COEUR

PhD period: 2005-2012
Promotors: P.J. Koudstaal and D.W.J. Dippel
Supervisor: E.G. Visch-Brink

1. PHD TRAINING

	Year	Workload (ECTS)
General Courses		
CPO-Mini course methodology and grant applications	2005	0.2
PhD day 2x	2006, 2009	0.2
Introduction to Data-analysis	2006	0.9
Regression Analysis	2006	1.4
Study Design	2006	4.3
Classical Methods for Data-analysis	2006	5.7
Good Clinical Practice	2007	0.7
Integrity in Research	2007	2.0
Short Introductory course on Statistics & Survival Analysis for MD's	2010	0.4
English Biomedical Writing and Communication	2011	4.0
Specific Courses		
Clinical cardiovascular epidemiology	2006	1.5
Vascular clinical epidemiology	2008	1.5
Clinical forum aphasia therapy	2006	0.1
PCDI Post-doc Retreat (Heeze)	2011	0.9
Aphasia Clinics: Primary Progressive Aphasia	2011	0.1
Aphasia Clinics: Complexity in aphasia therapy	2012	0.1
Innovations in Stroke Rehabilitation (Vancouver, Canada)	2012	0.3
Seminars and Workshops		
Seminars		
Neurologische Taal- en Spraakstoornissen (4 lectures)	2006-2009	0.4
Cardiovascular Clinical Epidemiology	2005	0.4
Neurovascular group: The role of brain edema in cerebral hemorrhage	2009	0.1
Alzheimer and Vascular cognitive impairment (Epidemiology)	2009	0.1
Neurovascular group: RATS-2	2009	0.1
Junior researchers	2009	0.1
Neurovascular group: Genomewide association studies of stroke	2009	0.1
CCMO-symposium: The safety of the participants in clinical research	2009	0.1
Neurovascular group: Blood pressure and vascular cognitive impairment	2010	0.1

Lab meeting prof.dr. M. Lambon Ralph (Erasmus MC)	2011	0.1
MIT results meeting (Rijndam Rehabilitation Center)	2012	0.1
Workshops		
Registration of clinical trials	2006	0.1
How to get published	2006	0.1
NWO workshops within the Mozaïek program: 4x	2006-2009	0.3
Workshop EndNote & literature search	2010	0.2

Presentations

Start meetings of the SPEAK-project in 8 regions in the Netherlands	2006-2007	1.2
CT-seminar Dutch Aphasia Foundation (Zwolle)	2007	0.2
Alumni Speech-Language Therapy Nijmegen	2008	0.1
Lab meeting dr. C. K. Thomson (Erasmus MC)	2008	0.1
Neurovascular group: Prognostic factors for the recovery of aphasia	2009	0.1
Results meeting SPEAK (Rotterdam)	2011	1.0
Lab meeting prof.dr. M. Lambon Ralph (Erasmus MC)	2011	0.1
Aphasia conference (Ede)	2011	0.1

(Inter)national Conferences

Academy of Aphasia, poster presentation (Amsterdam)	2005	1.2
Aphasiaforschung, poster presentation (Basel, Switzerland)	2005	1.2
NVN spring conference: Body and Perception (Utrecht)	2006	0.3
Junior aphasia researchers days, oral presentation (Groningen)	2006	0.9
Clinical Aphasiology Conference (Gent, Belgium)	2006	1.8
NVN 2nd Meeting of the European Societies of Neuropsychology (Toulouse, France)	2006	0.9
British Aphasiology Society Conference, oral presentation (Edinburgh, Scotland)	2007	1.5
Science of Aphasia VIII, poster presentation (Monopoli, Italy)	2007	1.5
Werkverband Amsterdamse Psycholinguïsten conference	2008	0.6
Academy of Aphasia, oral presentation (Montreal, Canada)	2011	1.5
Science of Aphasia VIII XIII, oral presentation (Groningen)	2012	1.5
ACRM-ASNR Progress in Rehabilitation Research Annual Conference, symposium presentation (Vancouver, Canada)	2012	2.0

2. TEACHING ACTIVITIES

	Year	Workload (ECTS)
Lecturing		
Werkgroep Commissie Therapie: Stichting Afasie Nederland (Utrecht)	2005	0.1
Neurologische Taal- en Spraakstoornissen (NTSS) (Erasmus MC)	2007	0.1
Meeting for speech-language therapists (Den Haag)	2007	0.1
Neurologische Taal- en Spraakstoornissen (NTSS) (Gent)	2008	0.1
Klinische Werkgroep van Stichting Afasie Nederland (Utrecht)	2007	0.1
Supervising Master's Theses		
Opleiding Logopedie Hogeschool Rotterdam (4 students	2006	0.4
Opleiding Logopedie Hogeschool Rotterdam (3 students)	2007	0.4
Opleiding Logopedie Hogeschool van Arnhem en Nijmegen (3 students)	2011	0.4
Supervising Research Internships		
Leiden University (5 students)	2008-2010	2.7
Erasmus MC University Medical Center, afstudeeronderzoek	2008-2009	0.8
Utrecht University (2 students)	2008-2010	1.0

3. OTHER

	Year	Workload (ECTS)
PhD day organizing committee	2012	0.6
Review of papers for international journals	2012	0.3
TOTAL WORKLOAD (ECTS)		**51.6**