MERVI JEHKONEN

The Role of Visual Neglect and Anosognosias in Functional Recovery After Right Hemisphere Stroke

ACADEMIC DISSERTATION
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University of Tampere
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P.O. Box 617
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Tel. +358 3 215 6055
Fax +358 3 215 7685
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ABSTRACT

The aim of this study was to evaluate some of the major diagnostic tools for the assessment of acute visual neglect and anosognosias for hemiparesis, for neglect and for illness, and to examine the impact of these defects on functional recovery during the first year after right hemisphere infarction. As clinicians it is important for us to be able to predict the natural course of recovery from visual neglect and anosognosias when making decisions on a patient’s abilities to manage at home or at work, and when evaluating a patient’s need for specific rehabilitation.

Between February 1994 and March 1998, 57 consecutive right hemisphere infarct patients under the age of 75 without previous neurological diseases or severe primary visual impairment were referred to neuropsychological examinations at the Department of Neurology and Rehabilitation, Tampere University Hospital. Acute neuropsychological examinations were carried out within 10 days of onset and the follow-up studies 3, 6 and twelve months later.

The results showed that on this particular set of patients: 1) the conventional subtests of the Behavioural Inattention Test (BIT) used to assess visual neglect share a common homogenous description, despite being the product of different mechanisms, as indicated by the double-dissociations between these subtests; 2) acute visual neglect can be reliably diagnosed with a combination of three subtests of the BIT (Line crossing, Letter cancellation and Line bisection); 3) anosognosias for neglect and for hemiparesis, as well as anosognosias for neglect and for illness, double-dissociated, indicating that anosognosia is not a unitary phenomenon; 4) predictors of functional outcome one year after stroke differed depending on the outcome measure applied: a) the patients’ recovery in basic activities of daily living evaluated by a neurologist and measured by a standardised scale, the Barthel Index, was best predicted by hemiparesis and visual neglect, b) self-evaluated functional outcome as measured by the Frenchay Activities Index, was best predicted by visual neglect and age, and c) the clinical outcome, namely time from stroke to discharge to home, as evaluated by a multidisciplinary team of the rehabilitation ward, was best predicted by hemiparesis, anosognosia for illness and the presence of a relative at home.

The present study highlights the importance of diagnosing visual neglect and anosognosias at the acute stage of stroke, since these deficits have predictive value for long-term recovery.
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<th>Description</th>
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<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>BI</td>
<td>Barthel Index</td>
</tr>
<tr>
<td>BIT</td>
<td>Behavioural Inattention Test</td>
</tr>
<tr>
<td>BITB</td>
<td>Behavioural subtests of the BIT</td>
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<td>BITC</td>
<td>Conventional subtests of the BIT</td>
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<tr>
<td>FAI</td>
<td>Frenchay Activities Index</td>
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<tr>
<td>FIM</td>
<td>Functional Independence Measure</td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
</tr>
<tr>
<td>SE</td>
<td>sensitivity of a test</td>
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<td>SP</td>
<td>specificity of a test</td>
</tr>
<tr>
<td>WAIS</td>
<td>Wechsler Adult Intelligence Scale</td>
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<td>WMS</td>
<td>Wechsler Memory Scale</td>
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1. INTRODUCTION

In most Western countries 2,000 people per one million of the population will suffer a stroke each year (Sudlow and Warlow 1997). One-third die over the next year, one-third remain permanently disabled and one-third make a reasonable recovery (Warlow et al. 1996). Stroke has been identified as the single most important cause of severe disability or invalidity in people living in their own homes (Murray and Lopez 1997; Grau 1999). In Finland, about 12,000 people develop a cerebrovascular disorder annually; 80% (about 9,600 people) have brain infarctions. About 70% (4,900) of the 7,000 stroke survivors can later manage at home, and one-fifth of them (980 people) return to work (Kaste et al. 2001).

Common physical deficits after a right hemisphere cerebrovascular accident are left motor and sensory defects as well as various cognitive deficits, including left-sided neglect, anosognosia, visuoconstructive and visuospatial disorders, motor inattention, dysprosody, disorders of body image and dressing, and visual memory deficits (Hier et al. 1983; Caplan and Bogousslavsky 1995; Lezak 1995). The most striking cognitive defect after right hemisphere damage is visual neglect, which means the failure of a patient to attend or respond to objects or people on the side opposite their brain lesion (Heilman et al. 1985b). Left neglect is also the most common neuropsychological deficit after right brain damage (Stone et al. 1993a; Ferro et al. 1999). Reports of the incidence of visual neglect in acute right hemisphere stroke patients vary considerably (13-85%) (Kinsella and Ford 1980; Denes et al. 1982; Hier et al. 1983; Vallar and Perani 1986; Levine et al. 1986; Fullerton et al. 1986; Sunderland et al. 1987; Stone et al. 1993a). Neglect is more severe and persistent following right than left brain damage (Bisiach et al. 1984; Fullerton et al. 1986; Weintraub and Mesulam 1988). The most common cause is cerebral infarction (Heilman et al. 1985b).

Another neuropsychological disorder found frequently after right hemisphere stroke is a lack of awareness of motor, visual, or cognitive deficits, called anosognosia (Starkstein et al. 1992; Stone et al. 1993a; Pedersen et al. 1996; Berti et al. 1996). The core deficit is unawareness, which may find expression in verbal denial or appropriate awareness of a deficit. Anosognosia can also manifest itself in patient’s behaviour (Berti et al. 1996). Anosognosia has been researched less intensively than visual neglect. Usually the term refers to general unawareness of illness or stroke, unawareness of hemiparesis or unawareness of hemianopia (Bisiach et al. 1986; Pedersen et al. 1996).

At present there is no agreement as to the formal evaluation of visual neglect in clinical practice, although numerous tests are available (Robertson and Halligan 1999). Routine clinical neurological assessments often fail to detect the specific problems attributable to visual neglect. A standardised test battery, the Behavioural Inattention Test (BIT; Wilson et al. 1987a, b), was introduced to provide clinicians with a more behaviourally relevant measure of visual neglect in peripersonal space (Robertson and Halligan 1999). This test is now widely used and therefore was chosen to evaluate the extent of visual neglect in this study.
The verbal questionnaires currently used to evaluate anosognosia are those proposed by Cutting (1978) and the rating scale (for anosognosia for hemiparesis and anosognosia for hemianopia) by Bisiach and associates (1986). Other instruments for assessing anosognosia have been developed (Anderson and Tranel 1989; Azouvi et al. 1996), but they have not been adopted widely. Since Cutting’s (1978) questionnaire was developed specifically for studying anosognosia in patients with hemiplegia after stroke, this was used together with the subquestions concerning the illness (stroke) in this study. Furthermore, an additional question to assess awareness of visual neglect was added for the purposes of the present study.

The long-term outcome of stroke has usually been studied with mixed or heterogenous groups including both left and right hemisphere damaged patients (e.g. Pedersen et al. 1996 and 1997; Paolucci et al. 1996a and 1998). Visual neglect in particular has been related to poor long-term recovery (e.g. Kinsella and Ford 1980 and 1985; Denes et al. 1982), although some controversial findings emphasise the contribution of anosognosia for hemiparesis and/or hemianopia to this poor functional outcome (Pedersen et al. 1996; Gialanella and Mattioli 1992).

The purpose of this thesis was to evaluate some of the major diagnostic tools currently employed to assess visual neglect and anosognosias after acute stroke and to see how good they are in predicting functional outcome during the first year after right hemisphere infarction. A homogenous group was selected to minimise confounding factors when examining the patients’ cognitive defects. It is well-known that aphasic disorders after left hemisphere damage make it difficult, sometimes even impossible, to evaluate cognitive functions in the acute phase. Neglect and anosognosia are common after right hemisphere stroke, but these deficits are more difficult to diagnose in the acute phase than aphasia or motor and sensory defects. However, visual neglect and anosognosias may have a significant role in predicting patients’ recovery.
2. REVIEW OF THE LITERATURE

2.1. Visual neglect

2.1.1. Definition and clinical picture of neglect

The first clinical descriptions of visual neglect were presented in the late 19th century by Hughlings Jackson 1876, Anton 1883, Pick 1898, Zingerle 1913 and Holmes 1918. The term “neglect” was first used by Pineas in 1931, although the specific features of visual neglect were not described until 1941 by Brain. The 1970s saw then a revival of the research interest (Halligan and Marshall 1993a).

Neglect is characterised by failure to orient, report, or respond to stimuli located predominantly on the side opposite to the site of the brain lesion, and the condition cannot be explained by sensory or motor deficits (Heilman et al. 1985b). Four basic, interrelated frames of reference define the description of “leftness” in a patient’s performance: a) egocentric (defined with respect to the subject; contains retino-, cephalo-, somatocentric and gravitational coordinates), b) world-centred (defined with respect to a fixed landmark, other than the subject’s body), c) allocentric (defined with respect to another extrapersonal object), and d) object-centred (defined with respect to a principal axis in the canonical representation on an object) (Halligan and Marshall 1993b; Mesulam 2000). Different spatial domains can be neglected without the involvement of other domains: 1) body (personal) space, 2) reaching (peripersonal) space, 3) far (extrapersonal) space, and 4) representational space (Robertson and Halligan 1999).

Most researchers agree that neglect consists of several related deficits, all of which exhibit predominantly lateralised disorder of attention when using and working in space (Robertson and Halligan 1999). Neglect is not a unitary disorder, but several subtypes have been reported (Halligan and Marshall 1994; Halligan and Marshall 1998a). It is considered to be a high-level cognitive deficit which may involve different sensory modalities (Robertson and Halligan 1999). The modality that has received most attention is visual neglect (Stone et al. 1993a), probably because it is the most dramatic and easily observable type of neglect (Mesulam 2000). The visual form of the disorder has also been at the centre of research in work to develop sensitive diagnostic methods.

In everyday life patients with neglect often fail to shave or dress the left side of their body, collide with objects to their left, omit the left parts of words when reading or writing, fail to attend to events and people situated on the left, and miss food on the left side of their plate. In more serious cases, neglect patients even fail to recognise their left extremities as their own. They show deviation of head, trunk and eyes towards the side of the lesion (i.e. right), especially in the acute phase. (Halligan and Marshall 1993a; Robertson and Halligan 1999)

Neglect may double-dissociate from hemiplegia, hemianopia and hemianesthesia, although these defects are often found in neglect patients (Vallar 1993). Moreover, neglect and anosognosia (for hemiparesis or visual field defect) and neglect and extinction have been reported to double-dissociate, as have different
aspects of neglect (Bisiach and Vallar 1988; Vallar 1993). In a group of 69 acute right hemisphere stroke patients, Stone and others (1998) examined the associations between neglect components (hemi-inattention, hemispatial or visual neglect, tactile extinction, allesthesia and hemiakinesia) and some related disorders (anosognosia, gaze paresis and visual field deficits). They found that anosognosia, as measured with Cutting’s (1978) questionnaire, correlated with gaze paresis and visual field deficits, but not with the main components of the neglect syndrome. Furthermore, double dissociations were reported between hemi-inattention and all other neglect components and related disorders, between tactile extinction and all other neglect components (except hemispatial or visual neglect), and between allesthesia and all other components. They concluded that neglect is a highly heterogenous syndrome and that its symptoms form a weak clinical syndrome, but not a functional one (Stone et al. 1998). In other words, visual neglect comprises damage to different components, none of which share a common underlying neural mechanism.

2.1.2. Theories and neuroanatomical correlates of neglect

The main theories of neglect, reviewed by Rizzolatti and Gallese (1988), propose that the main deficits of the disorder are: 1) a deficit of space perception, 2) a deficit of spatial attention (either concerning the intensive aspects of attention or the selective aspects of attention), and 3) a deficit in motor organisation (of responses towards certain parts of the personal and extrapersonal space). Furthermore, several authors have put forward a representational explanation of neglect (Bisiach and Luzzatti 1978; Halsband et al. 1985; Meador et al. 1987; Barbut and Gazzaniga 1987). They have found neglect in patients’ descriptions of mental images generated on the basis of information stored in memory.

Although neglect was formerly considered to be a sensory disorder and subsequently a disorder of spatial representation, there is now a growing consensus of opinion that it is best described as a defect of spatial attention (Mesulam 1994; Driver and Mattingley 1998; Hodgson and Kennard 2000). An attentional deficit is identified in a number of studies as a principal component in visual neglect (Heilman and Valenstein 1979; Riddoch and Humphreys 1983; Posner et al. 1984; Heilman et al. 1985a; Kinsbourne 1987; Mesulam 1990 and 2000).

The cerebral hemispheres have different roles in mediating the human individual’s attentional capacity. The right hemisphere directs attention more equally to both sides of the extrapersonal space and in both directions, whereas the left hemisphere directs attention mostly within the contralateral hemispace and in contraversive direction (Bisiach and Vallar 1988; Mesulam 2000). Therefore, florid contralateral neglect is seen almost exclusively after right hemispheric lesions (Mesulam 2000).

Mesulam (1990, 2000) considers neglect as a disorder of directed (selective) attention. He defines neglect as a deficit of an attentional network syndrome comprising three major components: sensory-representational (perceptual), motor-exploratory and limbic-motivational. The perceptual component means that sensory events occurring within the neglected hemispace lose their impact on awareness,
especially when competing sensory events take place in the contralateral space. The
motor-exploratory component reflects a deficiency to direct orienting and exploratory
behaviours into the neglected hemispace. Finally, the limbic-motivational component
of neglect emerges when a patient behaves as if nothing important could be expected
to happen in the left hemispace.

According to Mesulam (2000) directed attention is organised at the level of a
distributed large-scale network that contains three cortical components, namely the
posterior parietal component (sensory representation of the extrapersonal space), the
frontal component (the distribution of orienting and exploratory movements) and the
cingulate component (a map for assigning value to spatial coordinates). Since neglect
is seen as an “attentional network syndrome”, lesions within any component (the
parietal, the frontal, the cingulate) of this neural network or its interconnections (the
superior colliculus, the striatum, the thalamic pulvinar nucleus) can produce
contralesional neglect. The anatomical locations identified in Mesulam’s (2000) model
as being responsible for producing unilateral neglect have previously been singled out
by several authors (Heilman and Valenstein 1972; Kertesz and Dobrowolski 1981;
Vallar and Perani 1987; Ferro et al. 1987; Caplan et al. 1990; Bogousslavsky and
(1993) suggested that damage to any part of a complex cortico-subcortical neural
circuit consisting of the right inferior-posterior parietal regions, posterior and medial
portions of the thalamus, and the premotor frontal cortex, is responsible for producing
unilateral neglect. Some authors have reported a significant relationship between the
size of the hemispheric lesion and the severity or occurrence of neglect (Levine et al.
1986; Egelko et al. 1988).

2.1.3. Assessment of visual neglect (in peripersonal space)

During the period from 1944 to 1960 Zangwill and his collaborators developed several
methods for the assessment of visual neglect: these included clock drawing, pointing
tasks, and spontaneous drawing and copying tasks (Halligan and Marshall 1993a).
Traditionally neglect has been evaluated with paper-and-pencil tasks performed in the
peripersonal space, often “neglecting” the assessment of personal and far space. The
simplest and best-known ways of evaluating visual neglect are different copying,
drawing, line bisection, cancellation, reading and writing tasks (Pizzamiglio et al.
1992; Halligan and Marshall 1993a). In clinical practice, one of the most widely used
tests of visual neglect is a version of Albert’s (1973) line crossing test. Some research
groups employ specific tests for the evaluation of visual neglect. For example, in many
Italian studies (e.g. Antonucci et al. 1995; Paolucci et al. 1996a, b; Paolucci et al.
1998) visual neglect is evaluated with a screening battery of four tests: the Letter
Cancellation Test (Diller et al. 1974), the Barrage Test (Albert 1973), the Wundt-
Jastrow Area Illusion Test (Massironi et al. 1988) and the Sentence Reading Test
(Pizzamiglio et al. 1989).

According to Robertson and Halligan (1999) there are in all some 60 different
tests of visual neglect, most of which are variants of the clinically well established
bedside tasks (line bisection, cancellation, copying and drawing). However, it is
unlikely that any single test can provide a sufficient evaluation of all forms of visual neglect. The sensitivity of different neglect tests varies widely according to their ability to measure the different underlying deficits (Sunderland et al. 1987; Halligan et al. 1989; Pizzamiglio et al. 1992). Neglect may be evident in one of the tests but not in all of them at the same time. Moreover, there may be discrepancies between patients’ performance in standardised tests of visual neglect and in tasks simulating everyday activities (Zoccolotti and Judica 1991). It has also been found that neglect on clinical testing does not always generalise to daily activities and vice versa (Weinberg et al. 1977). Halligan et al. (1989) suggest that several tests are more likely to uncover evidence of neglect than a single test, but even so several studies (Denes et al. 1982; Fullerton et al. 1988; Friedman 1990; Halligan et al. 1992; Gialanella and Mattioli 1992; Blanc-Garin 1994; Pedersen et al. 1997) have applied only one test to assess the presence of visual neglect.

One of the most widely used test batteries in clinical practice and neglect research today is the Behavioural Inattention Test (BIT), which was developed and standardised by Wilson et al. (1987a, b). The BIT was designed to provide clinicians with a standard clinical assessment and ecologically valid measure of visual neglect in the peripersonal space. The BIT consists of two types of tests: six conventional (BITC) and nine behavioural (BITB) tests. It was standardised on 80 unselected stroke patients, 26 of whom had left brain damage and 54 right brain damage, and 50 age-matched controls (Halligan et al. 1991). On average the patients were evaluated two months poststroke. The presence of visual neglect (defined as impaired performance in the BITC tests) was found to be closely related to performance in the BITB subtests, which were constructed to provide more information about patients’ everyday problems (Wilson et al. 1987a, b).

In a related study, Halligan and others (1989) found in the same series (Halligan et al. 1991) of 80 stroke patients that the six BITC subtests showed high intercorrelations, and a factor analysis indicated that all tests loaded significantly on one factor. The patients were examined on average 85.5 days (range: 12-366 days) after the onset of stroke, i.e. they represented both the acute and postacute stages of illness. The single most sensitive BITC subtest was Star cancellation, but the authors suggested that several tests ought to be used when evaluating neglect in clinical settings. They concluded that visuospatial neglect as measured by the BIT is to a large extent a single phenomenon that measures aspects of the same, albeit robust, construct.

The BITC subtests that have traditionally been used in clinical neuropsychology to assess visual neglect, are Line cancellation, Letter cancellation, Star cancellation, Figure and shape copying, Line bisection, and Representational drawing. The BITB subtests are Picture scanning, Telephone dialling, Menu reading, Article reading, Telling and setting the time, Coin sorting, Address and sentence copying, Map navigation and Card sorting (Halligan et al. 1991). A modified version of the BIT specifically designed for acute stroke patients, has been validated and standardised by Stone et al. (1991a, b).

For the purposes of validation and standardisation of the modified BIT, Stone et al. (1991b) examined 44 consecutive patients of which 18 had right hemisphere
stroke. The patients were assessed with the modified BIT at three days after stroke. For patients having right hemisphere stroke the following seven subtests were presented: Pointing to objects located about the ward (which is not a part of the original BIT), Picture scanning, Menu reading, Article reading, Line cancellation, Star cancellation and Coin sorting. The most sensitive tests for detecting acute left neglect were Article reading, Star cancellation, Picture scanning and Line cancellation subtests. The authors concluded that the modified BIT is a valid and reliable test battery to detect, measure and monitor visuo-spatial neglect in acute stroke.

Although it is shown in several studies (Halligan et al. 1989; Pizzamiglio et al. 1992; Heilman et al. 1994; Halligan and Marshall 2001) that neglect is not a unitary disorder, the clinical assessment of neglect is commonly based on the assumption that it forms at least a weak clinical syndrome. This was confirmed in a group study of right hemisphere stroke patients by Stone et al. (1998). For purposes of clinical assessment the knowledge that the main components associate at least to some extent with each other is sufficient. However, this does not mean that the components of visual neglect share a single underlying neural mechanism, which would justify the definition of the defect as a functional syndrome (Stone et al. 1998).

2.2. Anosognosia

2.2.1. Definition of the concept

Anosognosia describes the lack of awareness of motor, visual or cognitive impairments in patients with neurological diseases (Berti et al. 1996). Anosognosia can occur independently at verbal and nonverbal behavioural levels (Berti et al. 1996; Vuilleumier 2000). This means, for example, that a patient who verbally denies his or her hemiplegia may accept staying in bed, but another patient who verbally admits his or her hemiplegia may attempt to walk, thus showing clearly inconsistent behaviours (Bisiach and Geminiani 1991; Berti et al. 1996; Vuilleumier 2000).

The first descriptions of anosognosia for hemiplegia were reported in the late 19th and early 20th century by Anton 1893, Pick 1898 and Zingerle 1913 (Bisiach 1999), but as Vuilleumier (2000) points out there have been earlier reports. In 1914 Babinski (quoted in Levine et al. 1991, Vuilleumier 2000) coined the term “anosognosia” to describe patients who appeared to be unaware of their hemiplegia. Like neglect, anosognosia is more frequent following right brain damage (Bisiach 1999).

It has been reported that anosognosia can exist for hemiplegia, cortical blindness (Anton’s syndrome), hemianopia, memory loss (amnesia), dementia and aphasia (McGlynn and Schacter 1989; Heilman et al. 1998). Anosognosia can occur without generalised intellectual impairment, confusion or diffuse brain damage (McGlynn and Schacter 1989; Bisiach and Geminiani 1991).

Anosognosia is traditionally defined as a lack of awareness of illness, as indicated by the patient’s verbal response when questioned (McGlynn and Schacter 1989; Berti et al. 1996; Vuilleumier 2000). According to McGlynn and Schacter (1989), “the very existence of neglect could be construed as a form of anosognosia,
inasmuch as unawareness (of the perceptual world) is a defining characteristic of the syndrome”. It is commonly assumed that a patient who, for example, shows florid visual neglect in drawing tasks, is not “aware” of his neglect, but as Halligan and Marshall (1998b) pointed out there are many patients with chronic neglect who have considerable conceptual and experiential insight into their deficit and its consequences.

Visual neglect and anosognosia are often associated in the acute phase of stroke, but they can also be dissociated from each other using existing clinical measures (Cutting 1978; Robertson and Halligan 1999). Moreover, anosognosia can be selective: patients with more than one neurological problem due to brain damage may be anosognosic for some problems but not for others (Bisiach and Geminiani 1991).

Bisiach and collaborators (1986) reported a double dissociation between unilateral neglect and unawareness of motor impairment, demonstrating that anosognosia for hemiplegia is not simply a reflection of unilateral neglect. Furthermore, anosognosia for hemiplegia double-dissociated from somato-sensory impairment and visual field defect, suggesting that these sensory defects are not essential conditions for anosognosia. Moreover, anosognosia for left hemianopia was double-dissociated from motor, somato-sensory and neglect disorders. Unawareness of hemiparesis and unawareness of hemianopia dissociated, but did not double-dissociate in the group studied by Bisiach et al. (1986).

2.2.2. Theories, incidence and neuroanatomical correlates of anosognosia

Heilman and others (1998) state that there are many different forms and degrees of unawareness; some patients might be unaware of one deficit and recognise another, equally disabling deficit. Neuroanatomically based theories attribute anosognosia either to focal brain lesions or to diffuse brain damage (McGlynn and Schacter 1989). Researchers who subscribe to the focal lesion explanation take the position that anosognosia results from damage to the right parietal lobe. On the other hand, anosognosia is considered a manifestation of a general mental disorder associated with diffuse brain damage.

McGlynn and Schacter (1989) suggested an integrative model in which unawareness of deficits could result from disruptions of either the posterior conscious awareness system (CAS) or the anterior executive system. Neuroanatomically, CAS is a posterior system involving the inferior parietal lobes and structures connecting them (cingulate area), and frontal regions constitute the executive system. The authors propose that unawareness of specific perceptual and motor deficits (anosognosia for hemianopia or anosognosia for hemiparesis) can occur with parietal damages, and unawareness of disorders of more complex functions (difficulties in problem-solving, or retrieval and integration of information) are associated with frontal damages.

Anosognosia is more common after right than left hemisphere stroke: the reported frequencies in right hemisphere strokes range from 28 to 85 % and in left hemisphere strokes from 0 to 17 % (Cutting 1978; Willanger et al. 1981; Hier et al. 1983; Motomura et al. 1988; Anderson and Tranel 1989; Starkstein et al. 1992; Stone et al. 1993a; Pedersen et al. 1996; Vuilleumier 2000). Anosognosia defined as the
denial of hemiparesis or hemianopia is a frequent disorder that is found in 17 - 28 % of all acute stroke patients (Stone et al. 1993a; Starkstein et al. 1993; Pedersen et al. 1996). Anosognosia for hemiplegia is predominantly found in patients with right-sided cerebral lesions (Caplan and Bogousslavsky 1995; Heilman et al. 1998).

In the study of Bisiach and colleagues (1986) anosognosia for left hemiplegia and that for left hemianopia were found in connection with both cortico-subcortical lesions and lesions confined to deep structures (the thalamus or the lenticular nucleus). The cortical lesions involved mostly the inferoposterior parietal cortex. Bisiach and Geminiani (1991) reported that no clear clinicoanatomical basis has been found for the dissociation of anosognosia for hemiparesis or for hemianopia. Frontal lobe damage can also produce disorders of awareness that are different in nature from disorders secondary to lesions in posterior or basal brain regions (Stuss 1991).

2.2.3. Assessment of anosognosia

Most of the existing clinical methods for the evaluation of anosognosia rely on verbal reports of subjective awareness rather than examining non-verbal, implicit awareness, which manifests itself in the patient’s behaviour (Diller and Riley 1993; Vuilleumier 2000). Verbal reports should not be considered the only means for evaluating unawareness of a deficit (Berti et al. 1996). The degree to which deficits are more obvious varies (e.g. a deficit which offers a continuous reminder to the patient experiencing it): for example, patients are more often aware of visible (e.g. motor) impairments than non-visible (e.g. cognitive) ones (Anderson and Tranel 1989). Some of the most common procedures for evaluating anosognosias are listed in Table 1.
<table>
<thead>
<tr>
<th>Author (year)</th>
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<th>Patient population</th>
<th>Forms of anosognosias assessed</th>
</tr>
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<tr>
<td>Nathanson et al. (1952)</td>
<td>Structured interview</td>
<td>Stroke</td>
<td>Verbal anosognosia for illness and hemiplegia</td>
</tr>
<tr>
<td>Cutting (1978)</td>
<td>Structured questionnaire</td>
<td>Stroke</td>
<td>Verbal anosognosia for illness and hemiplegia</td>
</tr>
<tr>
<td>Bisiach et al. (1986)</td>
<td>Rating scale</td>
<td>Stroke</td>
<td>Verbal anosognosia for hemiplegia and hemianopia</td>
</tr>
<tr>
<td>Anderson and Tranel (1989)</td>
<td>Structured interview</td>
<td>Stroke, dementia and head trauma</td>
<td>Verbal anosognosia for motor and cognitive defects (visual perception, language, memory, orientation and general intellect)</td>
</tr>
<tr>
<td>Berti et al. (1996)</td>
<td>Assessment of direct and indirect knowledge based on questioning and observation of patient’s behaviour</td>
<td>Stroke</td>
<td>Verbal and non-verbal anosognosia for hemiparesis and higher-order cognitive disabilities related to neglect</td>
</tr>
<tr>
<td>Azouvi et al. (1996)</td>
<td>Questionnaire</td>
<td>Stroke</td>
<td>Verbal awareness of everyday difficulties due to stroke</td>
</tr>
</tbody>
</table>
According to McGlynn and Schacter (1989) only a few researchers employ objective methods for assessing anosognosia. Nathanson and collaborators (1952) were among the first to develop a structured interview for purposes of assessing anosognosia (for stroke and for hemiplegia). The methods introduced by Cutting (1978) and Bisiach et al. (1986) are probably the best-known and most widely used in evaluating unawareness of illness, anosognosia for hemiparesis and anosognosia for hemianopia. Cutting’s (1978) questionnaire was developed for purposes of studying anosognosia in patients with hemiplegia after stroke. The instrument consists of general questions concerning the disease and specific questions concerning the affected limb. In the study of Bisiach and others (1986) anosognosia for motor impairment or visual field defect was assessed on a four-point rating scale.

Anderson and Tranel (1989) developed the Awareness Interview to evaluate awareness of cognitive and motor defects after cerebral infarction, dementia or head trauma. Operationally they defined unawareness as a discrepancy between the patient’s opinion of his/her abilities in the interview and his/her abilities as measured by neuropsychological and neurological examinations. The Awareness Interview comprises eight questions, each of which is evaluated on a three-point scale. The following domains are asked: 1) the patient’s opinion of why he/she is in hospital, 2) the presence of motor impairments, 3) the presence of cognitive defects in the areas of general thinking and intellect, orientation, memory, speech and language, and visual perception, and 4) the patient’s opinion of the quality of his/her performance in the tests and ability to return to normal activities. The Awareness Interview also takes into account awareness of visual perceptual problems, although the patient population in the study by Anderson and Tranel (1989) is a heterogenous one.

Berti and her colleagues (1996) have introduced an assessment procedure to evaluate different forms of anosognosia both verbally and in the patient’s actual behaviour. Their assessment procedure covers anosognosia for hemiparesis and unawareness of higher-order cognitive defects related to neglect disorders. They also specified two types of unawareness of neglect disorders, namely anosognosia for neglect dyslexia and anosognosia for drawing neglect (visual neglect).

Azouvi et al. (1996) presented the Catherine Bergego Scale (CBS) which consists of 10 items related to neglect in everyday life (e.g. dressing, washing, eating). Awareness of deficits is evaluated by asking patients about their difficulties in the CBS items. The anosognosia score is the difference between the examiner-evaluated score on the CBS scale and the patient’s self-evaluation.

For the purposes of the present study Cutting’s (1978) questionnaire was adopted since it was developed specifically for studying anosognosia in patients with hemiplegia after stroke and it consists of questions measuring both general unawareness of illness and anosognosia for hemiplegia. Furthermore, it is one of the most widely used anosognosia measures in previous studies. In the present study an additional question was also asked to assess awareness of visual neglect, even though it was recognised that patients can vary in their responses when only a single question is presented.
2.3. The relationship of neglect and anosognosias to functional outcome after stroke

Several authors have found that presence of neglect predicts poor recovery in everyday functioning and has profound effects on functional rehabilitation after stroke (Kinsella and Ford 1980; Denes et al. 1982; Kinsella and Ford 1985; Kotila et al. 1986; Fullerton et al. 1986; Fullerton et al. 1988; Stone et al. 1993b; Paolucci et al. 1996a; Paolucci et al. 1998; Katz et al. 1999; Cherney et al. 2001). A summary of some of the major functional outcome studies for stroke patients with special reference to visual neglect and/or anosognosia is presented in Table 2.
Table 2. Summary of functional outcome studies for stroke patients (RH=right hemisphere; LH=left hemisphere) with special reference to visual neglect and/or anosognosia

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number of lesion locations</th>
<th>Selection of patients</th>
<th>Follow-up times</th>
<th>Measures:</th>
<th>Main results</th>
</tr>
</thead>
</table>
| Kinsella and Ford (1980) | 14 RH 17 LH               | Selected group of patients referred to a rehabilitation hospital | 4, 8 and 12 weeks post-stroke    | a) Not described  
b) Not evaluated  
c) The Northwick Park Activities of Daily Living Index (Sheikh et al. 1979) | Visual neglect was associated with poor outcome at the 3-month follow-up.     |
| Denes et al. (1982)    | 24 RH 24 LH               | Selected group of patients with a motor deficit after stroke | At admission (on average 53 days after stroke) and 6 months post-stroke | a) The Copying Crosses Test (DeRenzi and Faglioni 1967)  
b) Based on observation of patient’s behaviour  
c) ADL scale of De Lagi et al. (1960) | Visual neglect was a significant predictor of poor outcome at six months. Anosognosia did not have an independent role in predicting outcome. |
| Kinsella and Ford (1985) | 14 RH 17 LH               | Selected group of patients referred to a rehabilitation hospital | 4 weeks, 8 weeks, 12 weeks and 18 months post-stroke | a) Albert’s test, a copy of complex figure of Rey, a copy of a Maltese cross and a flower, line bisection, and a tri-modal double simultaneous stimulation  
b) Not evaluated  
c) The Northwick Park Activities of Daily Living Index | Visual neglect was associated with poor outcome at the 18-month follow-up.     |
| Kotila et al. (1986)   | 20 RH 25 LH 11 brain stem stroke 10 with stroke NUD | Based on a stroke register in the Espoo-Kauniainen area in Finland | 3 months, one-year and four years after the onset | a) Copying a three-dimensional cross and a cube; refilling a cube, and two drawings  
b) Not evaluated  
c) 4-point scale of independence in ADL based on the clinician’s evaluation | The 4-year prognosis of patients still having visual neglect was poorer in ADL than that of patients without neglect. |
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number of lesion locations</th>
<th>Selection of patients</th>
<th>Follow-up times</th>
<th>Measures:</th>
<th>Main results</th>
</tr>
</thead>
</table>
| Fullerton et al. (1986) and Fullerton et al. (1988) | 88 RH 117 LH | Consecutive series | During the first 2 days after onset and 6 months later | a) Albert’s (1973) test  
b) Not evaluated  
c) 4-point scale of independence in ADL based on clinician’s evaluation | Visual neglect was a significant predictor of mortality and functional activity 6 months after stroke. |
| Gialanella and Mattioli (1992) | 45 RH | Selected group of patients with complete hemiplegia admitted to functional rehabilitation | 1 month and 5 months after stroke | a) Mesulam’s (1986) cancellation test  
b) Anosognosia for hemiplegia (Bisiach et al. 1986)  
c) Functional index (Tonazzi et al. 1986) | Anosognosia (for hemiplegia) was the worst prognostic factor for motor and functional recovery at 5 months. |
| Stone et al. (1993b) | 69 RH 102 LH | Consecutive series | 2-3 days, 3 months and 6 months after onset | a) The modified BIT (Stone et al. 1991a, b)  
b) Categorical: present / absent  
c) Barthel Index (Mahoney and Barthel 1965) | The degree of acute hemiparesis, the severity of acute neglect and the patient’s age were significant predictors of functional outcome at 3 and at 6 months. |
| Blanc-Garin (1994) | 49 RH 41 LH | Selected from referrals to a rehabilitation centre | On average 4 weeks post-stroke and at discharge | a) A letter cancellation task  
b) Not evaluated  
c) 9 items of basic ADL functions | General attentional factors had a role in patients’ functional recovery. |
| Pedersen et al. (1996) | 309 RH 257 LH | Consecutive series | During the first week after admission and thereafter weekly until discharge | a) Not evaluated  
b) Anosognosia for hemiparesis and for hemianopia (Bisiach et al. 1986)  
c) Barthel Index | Anosognosia was associated with poor functional outcome. |
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number of lesion locations</th>
<th>Selection of patients</th>
<th>Follow-up times</th>
<th>Measures:</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paolucci et al.</td>
<td>119 RH 136 LH (18 excluded)</td>
<td>Consecutive patients admitted to a rehabilitation hospital</td>
<td>At admission and at discharge.</td>
<td>a) A four-test battery (Pizzamiglio et al. 1989)</td>
<td>Patients with visual neglect had a significantly higher risk for poor autonomy in the Barthel Index than the rest of the patients.</td>
</tr>
<tr>
<td>(1996a)</td>
<td></td>
<td></td>
<td></td>
<td>b) Not evaluated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) Barthel Index</td>
<td></td>
</tr>
<tr>
<td>Pedersen et al.</td>
<td>307 RH 295 LH</td>
<td>Consecutive series</td>
<td>During the first week after admission and thereafter weekly until discharge</td>
<td>a) Circle cancellation test</td>
<td>Visual neglect per se had no negative prognostic influence on functional outcome.</td>
</tr>
<tr>
<td>(1997)</td>
<td></td>
<td></td>
<td></td>
<td>b) Anosognosia for hemiparesis and for hemianopia (Bisiach et al. 1986)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) Barthel Index</td>
<td></td>
</tr>
<tr>
<td>Paolucci et al.</td>
<td>206 RH 234 LH</td>
<td>Consecutive patients admitted to a rehabilitation hospital</td>
<td>At admission and at discharge.</td>
<td>a) A four-test battery (Pizzamiglio et al. 1989)</td>
<td>Visual neglect predicted poor functional recovery in both ADL and mobility.</td>
</tr>
<tr>
<td>(1998)</td>
<td></td>
<td></td>
<td></td>
<td>b) Not evaluated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) Barthel Index</td>
<td></td>
</tr>
<tr>
<td>Katz et al.</td>
<td>40 RH</td>
<td>Consecutive patients admitted to a rehabilitation hospital</td>
<td>Upon admission to rehabilitation, upon discharge from rehabilitation, and 6 months after discharge</td>
<td>a) The conventional subtests of the BIT</td>
<td>Patients with visual neglect had poorer outcome in the FIM than patients without neglect.</td>
</tr>
<tr>
<td>(1999)</td>
<td></td>
<td></td>
<td></td>
<td>b) Not evaluated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) The Functional Independence Measure (FIM; Granger et al. 1993)</td>
<td></td>
</tr>
<tr>
<td>Cherney et al.</td>
<td>52 RH</td>
<td>Consecutive patients referred to an acute inpatient rehabilitation facility</td>
<td>At admission, at discharge, and 3 months after discharge</td>
<td>a) The conventional subtests of the BIT</td>
<td>Patients with neglect had poorer functional outcome in the FIM than patients without neglect.</td>
</tr>
<tr>
<td>(2001)</td>
<td></td>
<td></td>
<td></td>
<td>b) Not evaluated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) The FIM</td>
<td></td>
</tr>
</tbody>
</table>
Kinsella and Ford (1980, 1985) found that hemi-inattention measured with a six-test battery at the one-month assessment was related to poorer level of functional ability defined with the Nordwick Park Activities of daily living (ADL) index by Sheikh et al. (1979) at the three- and 18-month follow-up. Their study group consisted of 14 right hemisphere and 17 left hemisphere stroke patients serially selected from referrals to a rehabilitation hospital.

According to Denes and colleagues (1982) neglect was the only significant predictor of ADL as evaluated by the comprehensive scale of De Lagi et al. (1960) that also takes into account outdoor activities. Their 48 patients, of whom 24 had right and 24 left hemisphere haemorrhagic or ischaemic stroke, were evaluated at admission (on average 53 days after stroke) and six months later. They assessed visual neglect with a single test involving copying of crosses. Anosagnosias for illness, for hemiplegia or for aphasia were also included in the assessment of emotional reactions, but they did not predict functional outcome.

Kotila and collaborators (1986) examined 66 patients three and twelve months after right or left hemisphere ischaemia or haemorrhagia. A follow-up was conducted four years after stroke. Visual neglect was evaluated by means of three unstandardised tests (two copying tasks and one drawing task). The outcome measure was a four-point classification describing independence or dependence in ADL. At the four-year follow-up 12 patients still had visual neglect and all of them remained more dependent in ADL than the rest of the patients. These 12 patients also had more severe and persistent hemiparesis at the acute stage than did the other patients.

Fullerton and others (1986) examined 205 unselected stroke patients (88 right and 117 left hemisphere stroke patients; no detailed description of the etiology was given) during the first two days after onset and six months later. Visual neglect was assessed with drawing and copying tests and Albert’s (1973) test. Functional recovery was determined on a four-point clinical scale: 1) complete recovery, 2) some disability, but independent in ADL, 3) dependent in ADL and 4) dead. They found that visual neglect was a significant predictor of functional recovery at six months. The authors suggested that visual neglect (the Albert test score) had independent predictive value, but the other predictors included (social, clinical, neurological and laboratory data) were not described in detail, nor were their possible associations with the neglect measure.

In a related study, Fullerton et al. (1988) found that visual neglect assessed with a single test by Albert (1973) was significantly related to outcome, but the possible associations between neglect and other significant predictors (leg function, arm power, level of consciousness, weighted mental score and electrocardiographic changes) were not reported in detail. It should be noted that 35% of the patients could not be adequately examined with the Albert test, and these missing values were estimated by the overall mean in the multivariate analysis.

Stone et al. (1993b) examined 171 consecutive acute stroke patients with left or right hemisphere ischaemia or haemorrhage at two to three days, three months and six months after onset. Visual neglect was assessed with the modified Behavioural Inattention Test (Stone et al. 1991a, b) and its severity measured by the Visual Neglect
Recovery Index (Stone et al. 1992). Functional outcome was evaluated with the Barthel Index (BI) by Mahoney and Barthel (1965). Only the outcome in stroke survivors was considered and the “dependent” patients were divided into three groups (mild, moderate, severe) according to the BI. The results indicated that the initial degree of hemiparesis, the severity of neglect and the patient’s age were significant predictors of functional outcome.

Paolucci and others (1996a) examined a group of 273 consecutive patients with acute left or right hemisphere haemorrhage or ischaemia, and found that hemineglect and the severity of stroke as measured by the Canadian Neurological Scale (Coté et al. 1989) at admission were the strongest predictors of poor functional outcome at discharge. Visual neglect was evaluated with a four-test battery (Pizzamiglio et al. 1989). In their study, patients with hemineglect had a significantly higher risk of poor autonomy in the Barthel Index, impaired mobility and a longer hospital stay than did the rest of the patients.

In another study, Paolucci and collaborators (1998) identified prognostic factors for “no”, “low” and “high” response to therapy in a group of 440 stroke patients suffering from either right or left cerebral ischaemia or haemorrhage and admitted to a rehabilitation centre for physical rehabilitation. Functional outcome in ADL was evaluated with the Barthel Index. They found that specific prognostic factors were associated with “no”, “low” and “high” therapeutic response in ADL and/or mobility. Their results indicated that patients without hemineglect had a better functional prognosis in both ADL and mobility. Anosognosia was not separately evaluated in the studies of Paolucci and associates (1996a, 1998).

Katz and associates (1999) studied 40 consecutive right hemisphere stroke patients suffering from vascular lesion and admitted to a rehabilitation hospital in order to evaluate the impact of visual neglect on the rehabilitation outcome and long-term functioning in ADL. Visual neglect was assessed with the BIT (the six conventional subtests) and outcome with the Functional Independence Measure (the FIM by Granger et al. 1993). Assessments were carried out upon admission to rehabilitation, upon discharge from the rehabilitation hospital, six months after discharge, and one year after onset. They found that the length of stay in the rehabilitation hospital was on average 40 days longer for patients with neglect than for patients without neglect. Moreover, neglect patients had poorer outcome in the FIM than did patients without neglect. They concluded that visual neglect was the major predictor of rehabilitation outcome in patients with right hemisphere stroke.

Cherney et al. (2001) examined 52 consecutive patients with right hemisphere stroke admitted to acute inpatient rehabilitation. The patients were assessed on admission to rehabilitation, at discharge and three months after. Visual neglect was assessed with the whole Behavioural Inattention Test (the BIT), but only the six conventional tests were used in the analyses. The FIM was used as the functional outcome measure. They found that patients with neglect stayed on average one week longer in inpatient rehabilitation than did patients without neglect. Furthermore, patients with neglect had poorer functional outcome than did patients without neglect. The authors pointed out that neglect may not be an independent predictor of poor
functional outcome because the confounding factors, namely age, time since onset and severity of motor impairment, were not taken into account.

In Blanc-Garin’s (1994) study general attention dysfunction but not hemineglect was found to be important for functional outcome as measured with nine items of basic ADL functions. She examined 90 rehabilitation patients suffering from right or left hemisphere infarction. Visual neglect was assessed with a letter cancellation task. Furthermore, two general attentional variables based on the letter cancellation task were assessed: 1) the “optimal” attentional level in the ipsilesional hemifield, and 2) the capacity to deal with the task when a cognitive load was added. Although visual neglect was related to poor ADL recovery, the author did not consider neglect to be a good predictor of recovery, but an indicator of impairment severity. The correlations obtained between ADL and attentional performance in the ipsilesional hemifield led the author conclude that general attentional factors have a role in predicting outcome.

Some authors (Gialanella and Mattioli 1992; Pedersen et al. 1996; Pedersen et al. 1997) propose that anosognosia instead of visual neglect might be an important predictor of poor outcome following right hemisphere stroke. Gialanella and Mattioli (1992) found in their series of 45 patients with right hemisphere stroke that the presence of anosognosia for hemiplegia as assessed by Bisiach’s and his coworkers’ (1986) method was the worst prognostic factor for motor and functional recovery from left hemiplegia one month after stroke. They examined personal and extrapersonal neglect and anosognosia for hemiparesis one and five months after onset. No other neuropsychological defects were studied. Only patients with severe left hemiplegia were included in their study, and extrapersonal (visual) neglect was assessed using a single cancellation task (Mesulam 1986). Functional recovery was assessed with an index (Tonazzi et al. 1986) measuring predominantly motor abilities. The authors concluded that extrapersonal neglect does not seem to be a negative predictor of motor and functional recovery, while anosognosia for hemiplegia, if still present one month after onset, worsened the prognosis of left hemiplegia. They were unable to establish whether anosognosia for hemiplegia was the main cause of poor recovery, or whether other factors associated with anosognosia were important.

Pedersen and others (1996) found in their series of 566 patients with acute left or right hemisphere stroke that the presence of anosognosia was associated with poor functional outcome: low BI score, a long stay in hospital, and reduced likelihood of discharge to independent living. Anosognosias for hemiparesis and for hemianopia were evaluated at the acute stage by the method of Bisiach and others (1986). Anosognosia for one or both of these defects was associated with severe strokes, large lesions and poor orientation. The authors concluded that anosognosia had an independent effect on functional outcome. However, only two other neuropsychological defects, namely orientation and aphasia as measured by the Scandinavian Neurological Stroke Scale (Scandinavian Stroke Study Group 1985; Lindenstrom et al. 1991), were included in their study.

In a related report, Pedersen and his collaborators (1997) concluded that hemineglect per se has no negative prognostic influence on functional outcome as
measured by the BI. This study group consisted of 602 consecutive stroke patients examined on admission. Visual neglect was assessed with a single cancellation task and anosognosia for hemiparesis and/or for hemianopia was evaluated using the procedure of Bisiach et al. (1986). Functional outcome was assessed by the BI during the first week after admission, every week during the hospital stay, and at discharge. An association was found between stroke severity and visual neglect, and also between visual neglect and anosognosia. The authors suggested that anosognosia had an independent value in the prediction of discharge BI score. In both studies by Pedersen et al. (1996, 1997) the two forms of anosognosias were treated together in the data analyses.

Denes et al. (1982) reported that anosognosia had no influence on outcome. Levine (1990) proposed that cognitive deficits often underlie persistent anosognosia for defects such as hemiplegia, and these deficits may play a role in determining the poor outcome of left hemiplegic patients with anosognosia.

Many studies emphasise the importance of visual neglect in predicting poor recovery after stroke, but the role of anosognosias still remains somewhat controversial. Moreover, the functional outcome of stroke patients has mostly been studied in mixed or heterogenous groups of patients including both left and right hemisphere patients. The methods applied in evaluating visual neglect, anosognosias and functional outcome vary widely. Furthermore, the possible associations or dissociations between visual neglect and anosognosias have not always been taken into account. The most important areas of debate are the various definitions used for visual neglect and anosognosias, the measures used for assessing visual neglect, anosognosias and functional outcome, the time interval between the onset of stroke and the first clinical evaluations, and the selection of patients (for example, the selected samples referred to rehabilitation centres versus those representing a consecutive series of patients in a certain district).
3. AIMS OF THE STUDY

This study had two general objectives: a) to evaluate some of the major diagnostic
tools for the assessment of visual neglect and anosognosias for illness, for hemiparesis
and for neglect in acute stroke, and b) to examine the relationship of visual neglect and
anosognosias to functional outcome during a one-year follow-up in a consecutive
series of patients with right hemisphere brain infarction. More specifically, answers
were sought to the following questions:

1. Do the six conventional tests for visual neglect included in the BIT measure defects
   that tend to associate strongly? What is the sensitivity and specificity of these tests
   and what provides the most time-efficient combination for the detection of visual
   neglect after a right hemisphere brain infarction? (Study I)

2. Do anosognosias for illness, for hemiparesis and/or for neglect dissociate from one
   another and are all these anosognosias associated with poor functional recovery
   after right hemisphere brain infarction? (Study III)

3. Does acute visual neglect after right hemisphere infarction predict poor recovery in
   ADL as evaluated by the Barthel Index during a one-year follow-up? What is the
   importance of visual neglect and anosognosias in this prediction in relation to other
   neurological and neuropsychological defects? (Additional analysis)

4. Does acute visual neglect after right hemisphere brain infarction predict poor
   functional recovery as evaluated by the patient him- or herself using the Frenchay
   Activities Index during a one-year follow-up? What is the importance of visual
   neglect and anosognosias in this prediction compared to other neurological and
   neuropsychological deficits? (Study II)

5. Does acute visual neglect after right hemisphere brain infarction predict a low rate
   of discharge to home? What is the importance of visual neglect and anosognosias
   in this prediction in relation to other neurological and neuropsychological deficits?
   (Study IV)
4. PATIENTS AND METHODS

4.1. Patients

Fifty-seven consecutive patients with acute right hemisphere brain infarction admitted to Tampere University Hospital as emergency cases were examined between February, 1994 and March, 1998. Brain infarct was established by computed tomography and magnetic resonance imaging. The following exclusion criteria were applied: history of neurological disorders, insufficient cooperation in the acute neuropsychological examination due to lowered level of consciousness, severe primary visual impairment, left-handedness and age over 75 years.

Neuropsychological and neuroradiological examinations were carried out within 10 days of onset (mean = 6.1, SD = 1.97, range = 2-10). Follow-up studies were conducted 3, 6 and twelve months after onset. None of the patients had recurrent stroke events during the 12-month follow-up. The patients’ characteristics at each examination are presented in Table 3.
Table 3. Patients’ characteristics at each examination

<table>
<thead>
<tr>
<th>Descriptive variables:</th>
<th>Follow-up times:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 days</td>
</tr>
<tr>
<td>Number of patients</td>
<td>56</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>20/36</td>
</tr>
<tr>
<td>BITC: N+</td>
<td>21 (35%)</td>
</tr>
<tr>
<td>BITB: N+</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>Hemiparesis: present</td>
<td>19 (34%)</td>
</tr>
<tr>
<td>Hemianopia: present</td>
<td>13 (23%)</td>
</tr>
<tr>
<td>Anelegc: present</td>
<td>14 (25%)</td>
</tr>
<tr>
<td>Ahemiparesis: present</td>
<td>8 (14%)</td>
</tr>
<tr>
<td>Aillness: present</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Age: mean (SD)</td>
<td>63.2 (10.2)</td>
</tr>
</tbody>
</table>

BITB = neglect diagnosis based on the behavioural subtests of the Behavioural Inattention test using the cutoff ≤ 67 for indicating an impairment
BITC = neglect diagnosis based on the failure in at least two of the conventional subtests of the Behavioural Inattention Test
N+ = neglect present
A = anosognosia
SD = standard deviation
$^1$ two patients (cases 17 and 52) showed fluctuation in their neglect diagnosis between the three- and six-month follow-ups
$^2$ two patients (cases 38 and 45) showed fluctuation in their neglect diagnosis between the six- and 12-month follow-ups
* fluctuation in the number of hemiparetic patients between the six- and 12-month follow-up is due to one patient’s score which changed from 0 (= normal motor functioning for hand and leg) to 2 (= mild motor dysfunction; 1 for hand function and 1 for leg function) without any recurrent stroke
The total numbers of patients and missing patients in each substudy are given in Tables 4 and 5.

### Table 4. Number of patients in the substudies I-IV

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
<th>New analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 days</td>
<td>52</td>
<td>56</td>
<td>56</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>3 months</td>
<td>-</td>
<td>53</td>
<td>53</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6 months</td>
<td>-</td>
<td>52</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12 months</td>
<td>-</td>
<td>50</td>
<td>49</td>
<td>49</td>
<td>43</td>
</tr>
</tbody>
</table>

### Table 5. Missing patients (case numbers) at each examination

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
<th>New analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 days</td>
<td>1(^a), 16(^d), 30(^a), 33(^a), 57(^a)</td>
<td>16(^d)</td>
<td>16(^d)</td>
<td>16(^d)</td>
<td>16(^d)</td>
</tr>
<tr>
<td>3 months</td>
<td>-</td>
<td>1(^a), 16(^d), 41(^b), 42(^b)</td>
<td>1(^a), 16(^d), 30(^a), 41(^b)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6 months</td>
<td>-</td>
<td>16(^d), 30(^a), 33(^a), 41(^b), 42(^c)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12 months</td>
<td>-</td>
<td>1(^a), 16(^d), 20(^b), 30(^c), 33(^c)</td>
<td>1(^a), 12(^b), 16(^d), 20(^b), 30(^c), 10(^c), 11(^c), 12(^c)</td>
<td>15(^a), 16(^d), 20(^b), 28(^b), 30(^c), 42(^c), 57(^e)</td>
<td>1(^a), 10(^c), 11(^c), 12(^c), 14(^c), 42(^c), 57(^e)</td>
</tr>
</tbody>
</table>

\(^a\) = partly incomplete examination due to fatigue or poor test motivation or partly missing data  
\(^b\) = died  
\(^c\) = refused to participate  
\(^d\) = developmental dyslexia  
\(^e\) = pons infarction

One patient (case 16) was excluded from all analyses because he had developmental dyslexia, which influenced his performance in some neglect tests. Two patients (cases 20 and 41) died during the 12-month follow-up, but they were included in Study IV because their discharge destinations were known. Three patients (cases 30, 33 and 42) refused to take part after the three-month follow-up. Five patients (cases 10, 11, 12, 28 and 57) had infarction in the pons and they were excluded from Study IV and from the additional analyses. The results concerning functional outcome (Studies II and IV) were analysed with or without the pons patients, and the results remained unchanged.

All patients volunteered to take part and gave their informed consent. The study was approved by the Ethical Committee of Tampere University Hospital.
4.2. Methods

4.2.1. Neuropsychological examination

An extensive neuropsychological examination was conducted for each patient 10 days, three months, six months and one year after stroke. The neuropsychological and outcome measures applied are listed in Table 6.

Table 6. Neuropsychological and outcome measures used in the substudies (Roman numerals refer to the original publications)

| Measures of visual neglect: (Wilson et al. 1987a, b; Halligan et al. 1991) |
| - BITC: (I-IV) |
| - BITB: (II-IV) |

| Measures of anosognosias: (III-IV) |
| - Cutting’s (1978) questionnaire: anosognosia for hemiparesis and anosognosia for illness |
| - Self-developed question: anosognosia for neglect |

| Measures of memory and orientation: (Wechsler 1945) |
| - Logical memory subtest of the Wechsler Memory Scale (WMS): verbal memory (II-IV) |
| - Visual reproduction subtest of WMS: visual memory (II) |
| - Orientation subtest of WMS: orientation (III) |

| Measure of visuospatial ability: (Wechsler 1981) |
| - Block Design subtest of the Wechsler Adult Intelligence Scale (WAIS) (II) |

| Measures of functional outcome: (II, IV) |
| - Barthel Index: a standardised scale measuring basic ADL functions (Mahoney and Barthel 1965) |
| - Frenchay Activities Index (Holbrook and Skilbeck 1983): patient’s subjective evaluation of outcome |
| - Time from stroke to discharge to home: a clinical outcome measure based on the decision of the multidisciplinary team of the rehabilitation ward |
4.2.1.1. Evaluation of neglect and setting criteria of an impairment (Studies I-IV)

Visual neglect was evaluated with a comprehensive battery of tests, the Behavioural Inattention Test (BIT), which has been standardised on stroke patients (Wilson et al. 1987a, b; Halligan et al. 1991; Studies I – IV). BIT consists of six conventional subtests (BITC) and nine behavioural subtests (BITB). The patients were divided into a neglect and a non-neglect group on the basis of the original cutoff scores for BITC (Studies I-IV) or BITB (Studies II-IV) (Wilson et al. 1987a, b; Halligan et al. 1991). The distribution of the BIT sum score was skewed, indicating that the majority of patients had little difficulty with the tests. Therefore the sum score was not used as a continuous variable. The neglect criteria for BITC were twofold: i) failure in at least two of the BITC subtests (Studies I, III and IV) or ii) sum score ≤ 129 (Study II). The number of neglect patients varied according to the criteria of impairment applied: criteria i) detected 21 neglect patients, and criteria ii) 16 neglect patients in the 10-day examination. The results of Study II were also analysed using criteria i) of BITC, but this did not affect the results. For the BITB subtests only the original criterion (sum score ≤ 67) was used.

The decision to apply the criterion of failure in at least two of the BITC subtests and not the original cutoff (≤ 129) for the sum score was based on the fact that the conventional tests are emphasised differently in the BIT sum score. For example, if a patient fails in Figure and shape copying test (cutoff: 3) and in Representational drawing (cutoff: 2), he still has a sum score of between 139 and 144, and will not be considered a neglect patient.

4.2.1.2. Assessment of anosognosias and the criterion of an impairment (Studies III and IV)

Verbal awareness or unawareness was assessed in relation to visual neglect, knowledge of stroke and hemiparesis. Unawareness of neglect was assessed by asking the patient: “Do you have any difficulties observing any part of the space around you?” If necessary, the patient was given the following alternatives: left side, right side, none or both sides. Before asking the question above, the questionnaire of Towle and Lincoln (1991) measuring everyday problems due to neglect was presented to the patient. The purpose of the questionnaire was to orientate the patient to the possible specific problems caused by neglect in order to make him or her understand the single question concerning unawareness of neglect.

Unawareness of illness and unawareness of hemiparesis were assessed using Cutting’s (1978) questions. Patients were considered to be unaware of illness if they gave inadequate answers to either of the two questions: “Why are you here?” and “What is the matter with you?” For example, when a patient who had a severe hemiplegia was asked the first question, she answered “No, I don’t know why I’m here, but I would really like to”. To the second question, her answer was: “I feel like I’m drunk.” Another patient, also with severe hemiplegia, when asked “What is the matter with you”, said “Nothing, but I would like to go for a walk.”
If patients with hemiparesis gave inadequate answers to any of the following seven questions, they were considered to be unaware of hemiparesis: “Is there anything wrong with your arm or leg?”; “Is it weak, paralysed or numb?”; “How does it feel?”; (Arm picked up) “What is this?”; “Can you lift it?”; “You clearly have some problem with this?”; (Asked to lift arms) “Can’t you see that your two arms are not at the same level?” For example, a patient with hemiplegia said that “No, my arm or my leg is not paralysed, there is nothing wrong with it.” When asked to lift his arm, he took hold of the researcher’s hand and lifted it, convinced it was his own left hand.

4.2.1.3. Evaluation of other cognitive functions (Studies II-IV)

Visual memory was assessed with the Visual Reproduction subtest (range = 0-14 points) and verbal memory with the Logical Memory subtest (range = 0-46 points) of the WMS (Wechsler 1945, 1975). Orientation was studied with the Orientation subtest (range = 0-5 points) of the WMS. Visuospatial abilities were evaluated using the Block Design subtest (range = 0-51 points) of the WAIS (Wechsler 1981, 1992). Raw scores of the Wechsler (Wechsler 1945, 1975, 1981, 1992) subtests were used.

4.2.2. Measurement of functional outcome (Studies II and IV)

4.2.2.1. The Barthel Index (Additional analysis)

Functional outcome in ADL was evaluated by a neurologist (Jukka-Pekka Ahonen or Gábor Molnár) with a standardised, widely used scale first introduced by Mahoney and Barthel (1965), the Barthel Index (BI). The BI consists of ten items: feeding, moving from wheelchair to bed and return, doing personal toilet, getting on and off toilet, bathing self, walking on a level surface (or propelling a wheelchair), ascending and descending stairs, dressing and undressing, continence of bowels and controlling bladder. The original scoring of the BI was used (range: 0-100).

4.2.2.2. The Frenchay Activities Index (Study II)

Functional outcome was measured with the Frenchay Activities Index (FAI) (Holbrook and Skilbeck 1983; Wade et al. 1985). The FAI consists of 15 items assessing three major factors: domestic chores, leisure and work, and outdoor activities. It measures independence and “social survival” at a higher level than ADL scales at the basic level of self-care. The FAI is a homogenous scale showing substantial validity with stroke patients and unselected groups of elderly subjects (Cockburn et al. 1990; Bond et al. 1992; Schuling et al. 1993). Wade (1998) describes the FAI as an extended ADL test which takes into account the wider community in which patients have to manage.

The outcome variable in the present study was the sum score of the 14 FAI items. Item 12 (gardening) was irrelevant for many patients and was therefore deleted. The possible range of scores in the original FAI is from 15 (poor functional ability) to 60 (good functional ability) points; in the reduced scale of this study it was from 14 to 56. The neuropsychologist read the questions to the patient and filled in the form according to the patient’s responses.
In the original FAI, the participants say how frequently (1 = not at all; 2 = less than once a week; 3 = once or twice a week; or 4 = almost daily) they have performed each of the 10 activities during the past three months and each of the five other activities during the past six months. In this study the patients estimated the frequency of each activity during the period from the stroke to the first follow-up examination and then from the previous to the present follow-up.

4.2.2.3. Discharge to home (Study IV)

In Study IV a third measure of functional outcome, namely discharge to home, was used. The outcome variable was the number of days from the onset of stroke to returning home. At our rehabilitation ward the decision to discharge a patient is made by a multidisciplinary team, who will want to see the patient reach a functional level that will allow him or her to cope at home. For clinical purposes, this outcome measure is certainly relevant.

4.2.3. Neurological and neuroradiological examinations (Studies I – IV)

A complete neurological examination including confrontational assessment of visual fields was performed in the acute phase and at each follow-up. The degree of motor defect and hemianopia was evaluated using the National Institute of Health Stroke Scale (Goldstein et al. 1989) at each time-point. Hemiparesis was scored using a scale from 0 (= normal) to 4 (= severe hemiparesis) for leg and arm separately, and these scores were summed to give a range from 0 to 8: 0 = no motor defect; 1-2 = mild hemiparesis; 3-5 = moderate hemiparesis, and 6-8 = severe hemiparesis. Visual field defect was scored as absent (= 0) or present (= 1).

All patients were examined with computed tomography (CT) and 53 patients additionally with magnetic resonance imaging (MRI) of the brain. On average the neuroradiological studies were carried out six days after onset (SD = 2.6; range = 0-12). The sizes of the infarctions were determined on the basis of T2 weighted MRI images by manual tracing or, when digital images were not available (n = 10), on the basis of the CT images using a method described by Broderick et al. (1993).

4.2.4. Statistical analyses

The data were described using means, standard deviations, medians or lower and upper quartiles for continuous variables and percentages for categorised variables.

A factor analysis (BMDP: principal component analysis) was computed for the BITC subtests to ascertain whether the severity of visual neglect could be measured as a unidimensional phenomenon. Diagnostic sensitivity and specificity were defined for each BITC subtest (Study I). Moreover, the dissociations and associations between the six conventional subtests of the BIT were examined using cross-tabulations (additional analysis).

Associations between awareness or unawareness of deficits and neurological or neuropsychological disorders themselves (hemiparesis and neglect) were described using cross-tabulations. t-tests for independent samples were used to compare
orientation, verbal memory and functional outcome (the FAI) in patients with and without different types of anosognosias (for hemiparesis, for neglect and for illness). Analysis of variance for repeated measures was used to evaluate possible change in verbal memory between different time-points and between patients with or without specific types of anosognosia (for hemiparesis, for neglect and/or for illness). (Study III)

Forward stepwise linear regression analyses were used to establish the possible predictive role of visual neglect for functional outcome (the FAI). The other predictive variables were patient’s age, hemiparesis, hemianopia, visuoconstructional ability, visual memory and verbal memory. (Study II)

Factors associated with discharge to home were identified by means of forward stepwise Cox model. The predictors were age, gender, presence of a relative, neglect (BITB and BITC), hemiparesis, verbal memory, unawareness of illness and size of infarct. (Study IV)

Additional analyses were done to examine the patients’ recovery in ADL as measured with the Barthel Index (BI). The BI was dichotomised using the median (= 100) as a cutoff point. Forward stepwise logistic regression analyses were used to find out the role of possible predictors (two visual neglect measures, age, gender, presence of a relative, hemiparesis, verbal memory, unawareness of illness and size of infarct) for poor functional outcome in the BI. Furthermore, to evaluate the independent effect of visual neglect and different forms of anosognosias to the three functional outcome measures (the BI, the FAI, discharge to home), matched pairs were formed. Matching was done for age and hemiparesis (for visual neglect and for anosognosia for neglect) or for age and visual neglect (for unawareness of illness) depending on the factor examined. Wilcoxon’s test was used to evaluate the differences in the three functional outcome measures between the matched pairs.

The computations were carried out using BMDP statistical software (version 1990) on a SUN/UNIX mainframe and SPSS/Win (versions 6.0, 8.0 and 9.0) on a personal computer.
5. RESULTS

5.1. Assessment of acute neglect (Study I and additional analysis)

The purpose of this study was to examine the possible associations and/or dissociations between the visual neglect tests, and to find a simplified screening method for the evaluation of acute visual neglect. Therefore, all the BITC subtests were analysed separately according to their associations or dissociations, and diagnostic sensitivities and specificities.

Table 7 describes the patients’ characteristics in Study I. Five patients were excluded: one had developmental dyslexia and four patients had partly incomplete data due to fatigue or poor test motivation. One neglect patient (case 30) was excluded from Study I because he could not carry out the behavioural subtests of the BIT due to fatigue. In additional analyses his results in the conventional subtests of the BIT were used.

Table 7. Patients’ characteristics at the 10-day examination in Study I

<table>
<thead>
<tr>
<th>Descriptive variables</th>
<th>Patients with neglect</th>
<th>Patients without neglect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of patients</td>
<td>20 (38.5%)</td>
<td>32 (61.5%)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>11/9</td>
<td>22/10</td>
</tr>
<tr>
<td>Hemianopia: present</td>
<td>7 (35%)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Hemiparesis: present</td>
<td>12 (60%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Age: mean (SD)</td>
<td>60.8 (10.4)</td>
<td>64.7 (10.2)</td>
</tr>
<tr>
<td>Education in years: mean (SD)</td>
<td>8.1 (1.4)</td>
<td>8.2 (1.9)</td>
</tr>
</tbody>
</table>

The dissociations and associations between the conventional subtests of the BIT were examined in detail in the neglect group (n=21). The results are described in Table 8.
Table 8. Dissociations and associations between the conventional subtests of the BIT

<table>
<thead>
<tr>
<th>Subtests:</th>
<th>LiC</th>
<th>LeC</th>
<th>SC</th>
<th>Cop</th>
<th>LiB</th>
<th>Dr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>LiC</td>
<td>-</td>
<td></td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>2</td>
<td>11</td>
<td>1</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>LeC</td>
<td>-</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>2</td>
<td>13</td>
<td>2</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>SC</td>
<td>-</td>
<td></td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>3</td>
<td>14</td>
<td>6</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Cop</td>
<td>-</td>
<td></td>
<td></td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>8</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>LiB</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Dr</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

+ = neglect present
- = neglect absent
LiC = Line crossing
LeC = Letter cancellation
SC = Star cancellation
Cop = Figure and shape copying
LiB = Line bisection
Dr = Representational drawing

Double dissociations were found between all the conventional subtests of the BIT, which means that in each test there was at least one patient who failed in subtest A, but succeeded in subtest B, and another patient who failed in subtest B, but not in A. Therefore, it is not sufficient to measure visual neglect by any single conventional test.

In the present study, the criterion of failure in at least two of the BITC subtests was used for diagnosing visual neglect. A factor analysis showed that each of the BITC subtests had high loadings on the factor that accounted for 85% of their total variance (Table 9). The results indicated that the conventional subtests share a common homogenous description, despite being the product of different mechanisms, as indicated by the double dissociations.
Table 9. Unrotated first factor of the BITC subtest in the total series (N=52)

<table>
<thead>
<tr>
<th>BITC subtests</th>
<th>Loading on factor 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line crossing</td>
<td>0.96</td>
</tr>
<tr>
<td>Star cancellation</td>
<td>0.96</td>
</tr>
<tr>
<td>Letter cancellation</td>
<td>0.94</td>
</tr>
<tr>
<td>Line bisection</td>
<td>0.89</td>
</tr>
<tr>
<td>Representational drawing</td>
<td>0.89</td>
</tr>
<tr>
<td>Figure and shape copying</td>
<td>0.89</td>
</tr>
<tr>
<td>Eigenvalue</td>
<td>5.12</td>
</tr>
<tr>
<td>Percentage of variance</td>
<td>85.4</td>
</tr>
</tbody>
</table>

The sensitivities (SE) and specificities (SP) of the BITC subtests varied. The best single BITC subtest for detecting acute neglect was the Star cancellation test with a SE of 80 % and a SP of 91 %. A three-test combination, namely Line crossing, Letter cancellation and Line bisection, is needed to detect visual neglect in acute stroke (SE: 95 % and SP: 97 %). This combination failed to identify only one patient in the neglect group and one patient in the non-neglect group.

5.2. Dissociations between anosognosia for illness, anosognosia for hemiparesis and anosognosia for neglect (Study III)

The aim of Study III was to find out whether different anosognosias co-occur or whether they dissociate. The study group comprised 56 patients in the acute phase, 53 patients in the three-month examination and 49 patients in the 12-month examination. One patient was excluded from the 10-day examination (dyslexia), four patients were missing from the three-month examination (1 dyslexia, 3 incomplete data), and eight patients from the 12-month examination (1 dyslexia, 2 incomplete data, 2 died and 3 refused to participate).

Anosognosia for neglect and anosognosia for hemiparesis double-dissociated in the 10-day examination. A double dissociation of anosognosia for neglect and unawareness of illness was also found. Unawareness of illness and anosognosia for hemiparesis dissociated, but did not double-dissociate. The dissociations of different anosognosias are shown in Table 10.
Table 10. The associations and dissociations between different anosognosias (A). (Figures in boldface indicate the double dissociations)

<table>
<thead>
<tr>
<th>Form of anosognosia:</th>
<th>$A_{\text{neglect}}$</th>
<th>$A_{\text{hemiparesis}}$</th>
<th>$A_{\text{illness}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- +</td>
<td>- +</td>
<td>- +</td>
</tr>
<tr>
<td>$A_{\text{neglect}}$</td>
<td>-</td>
<td>2 4</td>
<td>5 2</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>3 4</td>
<td>10 4</td>
</tr>
<tr>
<td>$A_{\text{hemiparesis}}$</td>
<td>-</td>
<td></td>
<td>5 -</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td>4 4</td>
</tr>
<tr>
<td>$A_{\text{illness}}$</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Three patients were unaware of visual neglect and aware of hemiparesis. Two of them had severe neglect with poor results in the Orientation and Logical Memory tests, and one had moderate neglect with normal results in the Orientation and Logical Memory tests. Four patients had anosognosia for hemiparesis, but were aware of neglect. All these four patients had severe hemiparesis and severe neglect, and two of them had normal performance in the Orientation and Logical Memory tests.

Ten patients were unaware of neglect but aware of stroke. Of these ten patients, one had severe neglect with normal performance in the Orientation and Logical Memory tests. Two patients had anosognosia for illness but recognised their severe neglect. These two patients had normal orientation, and one of them had normal performance in the Logical Memory test.

The anosognosic patients’ characteristics are presented in Table 11.
Table 11. Description of the patients anosognosic for illness, for neglect or for hemiparesis on major variables in relation to awareness of defects

<table>
<thead>
<tr>
<th>Descriptive variables:</th>
<th>$A_{\text{illness}}$ (n=6)</th>
<th>$A_{\text{neglect}}$ (n=14)</th>
<th>$A_{\text{hemiparesis}}$ (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: mean (SD)</td>
<td>65.5 (6.5)</td>
<td>60.7 (11.1)</td>
<td>66.1 (6.6)</td>
</tr>
<tr>
<td>Orientation: mean (SD)</td>
<td>4.2 (1.0)</td>
<td>4.1 (1.0)</td>
<td>4.4 (0.9)</td>
</tr>
<tr>
<td>Verbal memory: mean (SD)</td>
<td>14.0 (6.0)</td>
<td>17.9 (5.9)</td>
<td>14.4 (6.5)</td>
</tr>
<tr>
<td>Neglect (BITC): mean (SD)</td>
<td>62.0 (57.4)</td>
<td>96.1 (40.3)</td>
<td>43.6 (43.6)</td>
</tr>
<tr>
<td>Hemiparesis: mean (SD)</td>
<td>4.0 (3.5)</td>
<td>3.2 (3.6)</td>
<td>6.9 (1.6)</td>
</tr>
<tr>
<td>Hemianopia: present</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

BITC = the conventional subtests of the Behavioural Inattention Test; failure in at least two of the conventional subtests was considered indicative of neglect

Orientation: raw score of the WMS Orientation subtest (range: 0-5; 0 = disorientation; 5 = intact orientation)

Verbal memory: raw score of the WMS Logical Memory subtest (range: 0-46)

Hemiparesis: NIH Stroke Scale sum score for paresis of the leg and the arm (range: 0-8; 0 = no motor dysfunction; 8 = severe hemiparesis)

SD = standard deviation

There was at least one patient with normal performance in the Orientation and Logical Memory tests in each group involving double dissociations. This demonstrates that general cognitive dysfunction was not a necessary condition for anosognosias or for their double dissociations.

5.3. Acute visual neglect and anosognosias as predictors of functional outcome during a one-year follow-up (Studies II, IV, additional analysis)

5.3.1. Barthel Index: a standardised outcome measure

The Barthel Index (the BI by Mahoney and Barthel 1965) was used to provide an objective functional outcome measure for basic ADL. The BI is a standardised, widely used outcome measure and has been classified as a scale that measures purely ADL (Wade 1998).

In the present study, the patient’s BI sum score at the one-year follow-up was used as an outcome variable. The sum score was dichotomised using the cutoff point of 100, which means complete recovery in basic ADL. The predictors were age, gender, presence of a relative (a person living with the patient), visual neglect, hemiparesis, verbal memory, unawareness of illness and size of infarct.

The predictive significance of each variable separately was determined using the logistic regression model. Thereafter the best set of predictors was computed using the forward stepwise logistic regression model (probability of F to enter = 0.05 and probability of F to remove = 0.10). Table 12 shows the significance of each predictor alone. Neglect (BITC and BITB), hemiparesis, size of infarction and unawareness of
illness were statistically significant single predictors. Each of them were related to poor functional outcome as measured with the BI at the one-year follow-up.

Table 12. Prediction of functional outcome (the Barthel Index) at one-year follow-up with each predictor variable separately (N = 43)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI for OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neglect (BITB)</td>
<td>67.47</td>
<td>(8.29; 549.10)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>25.78</td>
<td>(4.34; 153.08)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neglect (BITC)</td>
<td>30.00</td>
<td>(3.31; 272.34)</td>
<td>0.003</td>
</tr>
<tr>
<td>Size of infarction</td>
<td>1.02</td>
<td>(1.01; 1.04)</td>
<td>0.007</td>
</tr>
<tr>
<td>Unawareness of illness</td>
<td>17.71</td>
<td>(1.71; 183.83)</td>
<td>0.016</td>
</tr>
<tr>
<td>Gender (F vs. M)</td>
<td>1.59</td>
<td>(0.40; 6.41)</td>
<td>0.51</td>
</tr>
<tr>
<td>Verbal memory (WMS)</td>
<td>0.94</td>
<td>(0.85; 1.05)</td>
<td>0.30</td>
</tr>
<tr>
<td>Relative at home</td>
<td>0.49</td>
<td>(0.11; 2.17)</td>
<td>0.35</td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>(0.94; 1.06)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

BITC = the conventional subtests of the Behavioural Inattention Test; patients scoring under the cutoff in at least two of the BITC subtests were considered neglect patients
BITB = the behavioural subtests of the Behavioural Inattention Test; patients scoring under the cutoff (67) were considered neglect patients
WMS = Wechsler Memory Scale; Logical Memory subtest
OR = odds ratio
CI = confidence interval

When age, gender, neglect (BITC or BITB separately), hemiparesis, size of infarction, unawareness of illness, verbal memory and presence of a relative were used as possible predictors in the model, the best combination of predictors was hemiparesis and neglect (BITC) or neglect alone (BITB) (Table 13).
Table 13. Best set of predictors in acute right hemisphere infarct for functional outcome at one year measured with the Barthel Index (N = 43)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>95% CI for OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>9.02</td>
<td>(1.24; 65.47)</td>
<td>0.04</td>
</tr>
<tr>
<td>Neglect (BITC)</td>
<td>11.67</td>
<td>(1.06; 127.83)</td>
<td>0.03</td>
</tr>
<tr>
<td>Model II:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neglect (BITB)</td>
<td>67.47</td>
<td>(8.29; 549.10)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

BITC = the conventional subtests of the Behavioural Inattention Test; patients scoring under the cutoff in at least two of the BITC subtests were considered neglect patients
BITB = the behavioural subtests of the Behavioural Inattention Test; patients scoring under the cutoff (67) were considered neglect patients
OR = odds ratio
CI = confidence interval
Model I: only BITC of the two neglect variables was included in the model
Model II: only BITB of the two neglect variables was included in the model

Analyses were also done to establish the predictive value of anosognosia for neglect and anosognosia for hemiparesis to functional outcome. First, analyses were carried out separately for neglect patients (n = 18 according to BITC) and for hemiparetic patients (n = 11). The patients who were aware of the deficit (neglect or hemiparesis) were compared to those patients who were not (= anosognosic patients). The results indicated that neither anosognosia for neglect (OR = 0.21; p = 0.22; 95% CI: 0.02 - 2.48) nor anosognosia for hemiparesis (OR = 3.33; p = 0.40; 95% CI: 0.20 - 54.52) was a significant predictor of one-year functional outcome as measured with the BI. Secondly, anosognosia for hemiparesis as a predictor was also studied in the total series of 43 patients. The other predictors were the same as in Table 12. The results showed that hemiparesis and visual neglect (BITC) (OR = 10.65; p = 0.06; 95% CI: 0.94 - 120.18) were the best predictors for functional outcome at one year. Hemiparesis was a significant predictor, but anosognosia for hemiparesis had no independent predictive value (“hemiparesis without anosognosia” compared to “no hemiparesis” OR = 6.35; 95% CI: 0.58 - 69.34 and “hemiparesis with anosognosia” compared to “no hemiparesis” OR = 13.3; 95% CI: 0.97 - 183.37).

5.3.2. Predictors of patient’s self-evaluated outcome: the Frenchay Activities Index (Study II)

The aim of Study II was to examine the predictive value of acute neglect for functional outcome at 3, 6 and twelve months after stroke. Special attention was paid to the possible additional value of neglect measures (BITB and BITC) besides hemiparesis,
hemianopia, cognitive deficits and age. All the predictors were determined at the acute stage. Functional outcome was evaluated with the FAI based on the patient’s self-evaluation of the frequency of various activities. The patients’ characteristics in Study II are presented in Table 14.

Table 14. Patients’ demographic and clinical characteristics at each time-point in Study II

<table>
<thead>
<tr>
<th>Descriptive variables</th>
<th>Follow-up times:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 days</td>
</tr>
<tr>
<td>Number of patients</td>
<td>56</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>20/36</td>
</tr>
<tr>
<td>Hemianopia: present</td>
<td>13 (23%)</td>
</tr>
<tr>
<td>Hemiparesis: present</td>
<td>19 (34%)</td>
</tr>
<tr>
<td>BITB: N+</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>BITC: N+</td>
<td>16 (29%)</td>
</tr>
<tr>
<td>Age: mean (SD)</td>
<td>63.23 (10.21)</td>
</tr>
<tr>
<td>Visual memory: Mean (SD)</td>
<td>4.70 (3.52)</td>
</tr>
<tr>
<td>Verbal memory: Mean (SD)</td>
<td>19.77 (6.35)</td>
</tr>
<tr>
<td>Block Design: Mean (SD)</td>
<td>12.41 (10.61)</td>
</tr>
<tr>
<td>Mean (SD) **n=55</td>
<td></td>
</tr>
</tbody>
</table>

BITB = dichotomy of the behavioural subtests of the Behavioural Inattention Test; the criterion for neglect was the cutoff score for the BITB sum score ≤ 67
BITC = dichotomy of the conventional subtests of the Behavioural Inattention Test; the criterion for neglect was the cutoff score for the BITC sum score ≤ 129
SD = standard deviation
N+ = neglect patients
* fluctuation in the number of hemiparetic patients between the six- and twelve-month follow-up is due to one patient’s score which changed from 0 (= normal motor functioning; 0 for hand and 0 for leg function) to 2 (= mild motor dysfunction; 1 for hand function and 1 for leg function) without any recurrent stroke event
**one case (42) missing due to poor test cooperation

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The results indicated that neglect (BITB) was the best single predictor of functional outcome. Together with age, it formed the best combination of predictors for poor functional outcome at each follow-up. Hemiparesis was included in the model at three months, but other predictors (hemianopia, BITC, visuoconstructional and memory deficits) had no additional predictive value.
However, it is important to note that neglect recovered soon. At the 12-month follow-up there were only three neglect patients according to BITB criteria in contrast to 15 at the acute phase (Table 14). Residual neglect which cannot be detected by means of neuropsychological tests, may thus cause difficulties in ADL during the follow-up.

5.3.3. Predictors of discharge to home (Study IV)

In Study IV another type of functional outcome measure was used, namely discharge to home. The outcome variable was the time in days from stroke to discharge to home. The predictors were age, gender, size of infarct, neglect (BITB and BITC), hemiparesis, verbal memory, unawareness of illness, anosognosia for neglect, anosognosia for hemiparesis and presence of a relative at home. The follow-up time was one year. The aim was to study factors at the acute stage of stroke related to discharge to home, with special reference to the possible role of anosognosias.

The study group comprised 56 patients at the 10-day examination (1 missing patient due to dyslexia) and 49 patients at the 12-month examination (8 missing patients: 1 dyslexia, 5 pons infarction, 2 refused to participate).

Neglect (both BITB and BITC), hemiparesis, size of infarction, unawareness of illness, verbal memory and gender were all statistically significant single predictors. The best set of predictors for discharge to home was hemiparesis, unawareness of illness and presence of a relative at home. Unawareness of illness and hemiparesis lengthened the hospital stay, while the presence of a relative shortened it.

Unpublished data concerning the length of hospital stay are summarised in Table 15. The median duration of the hospital stay for the whole patient group (n = 47) was 10 days (Q1 = 4; Q3 = 44). Two patients (cases 34 and 41) were excluded because they did not return to home during the one-year follow-up. Patients with acute hemiparesis (median = 66 days; lower quartile Q1 = 56; upper quartile Q3 = 122), unawareness of illness (median = 82 days; Q1 = 42; Q3 = 160), or visual neglect in BITC (median = 52 days; Q1 = 10; Q3 = 106) remained in hospital much longer than did patients without these disorders (patients without hemiparesis: median = 8 days (6; 17); patients aware of illness: median = 9 days (6; 29), and non-neglect patients: median = 8 days (6; 18). The presence of a relative at home shortened the length of hospital stay in relation to all of the most important predictors, namely hemiparesis, unawareness of illness and neglect in BITC.
Table 15. Length of hospital stay (in days) according to the most important predictors in the acute phase and in relation to the presence or absence of a relative at home (N = 47)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Length of hospital stay: median (Q1; Q3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative: yes</td>
</tr>
<tr>
<td></td>
<td>n = 35</td>
</tr>
<tr>
<td>Hemiparesis: -</td>
<td>7 (5; 9)</td>
</tr>
<tr>
<td></td>
<td>n = 26</td>
</tr>
<tr>
<td>Hemiparesis: +</td>
<td>65 (41; 88)</td>
</tr>
<tr>
<td></td>
<td>n = 9</td>
</tr>
<tr>
<td>Unawareness: -</td>
<td>8 (6; 25)</td>
</tr>
<tr>
<td></td>
<td>n = 33</td>
</tr>
<tr>
<td>Unawareness: +</td>
<td>46 (38; NA)</td>
</tr>
<tr>
<td></td>
<td>n = 2</td>
</tr>
<tr>
<td>Neglect: -</td>
<td>7 (5; 9)</td>
</tr>
<tr>
<td></td>
<td>n = 24</td>
</tr>
<tr>
<td>Neglect in BITC: +</td>
<td>53 (10; 74)</td>
</tr>
<tr>
<td></td>
<td>n = 11</td>
</tr>
<tr>
<td>Total:</td>
<td>8 (6; 35)</td>
</tr>
<tr>
<td>N = 47</td>
<td>n = 35</td>
</tr>
</tbody>
</table>

Q₁ = lower quartile  
Q₃ = upper quartile  
- = absent  
+ = present  
NA = not available  
Unawareness: refers to unawareness of illness  
BITC = the conventional subtests of the Behavioural Inattention Test; patients scoring under the cutoff in at least two of the BITC subtests were considered neglect patients

Neglect variables (BITB and BITC) were closely associated with unawareness of illness. All patients who were unaware of illness at the acute phase (n = 6) also had neglect. This association explains why neglect was not included in the set of best predictors.

None of the patients was unaware of illness three months after the stroke. This means that unawareness of illness cannot be the cause of long-term dependence on constant help in everyday life. It is more likely that unawareness of illness is an indicator of severe stroke that causes persistent cognitive deficits. The results suggest that motor functioning is the most important factor in the evaluation of patients’ discharge to home at the acute stage of stroke. The only cognitive factor emerging as an important predictor of discharge to home was unawareness of illness.
5.3.4. The independent role of visual neglect and anosognosias in the functional outcome measures (Additional analysis)

a) Visual neglect

To evaluate the independent effect of visual neglect upon the functional outcome measures (the BI, the FAI, and discharge time), matched pairs with and without neglect were formed. Matching was done for age and hemiparesis. For age, a maximum difference of five years was allowed. For hemiparesis both subjects in the pairs either had or did not have the defect. Nine pairs were found (Table 16).

Table 16. Descriptive data of the matched pairs (neglect (N+) vs. non-neglect patients (N-)) in relation to age, hemiparesis and the three functional outcome measures (the Barthel Index (BI), the Frenchay Activities Index (FAI) and discharge time in days) (N = 18)

<table>
<thead>
<tr>
<th>Matched pairs</th>
<th>Hemiparesis</th>
<th>Age</th>
<th>BI score</th>
<th>FAI score</th>
<th>Discharge time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N+ N-</td>
<td>N+ N-</td>
<td>N+ N-</td>
<td>N+ N-</td>
<td>N+ N-</td>
</tr>
<tr>
<td>Pair 1</td>
<td>+ +</td>
<td>57 54</td>
<td>80 100</td>
<td>28 38</td>
<td>65 8</td>
</tr>
<tr>
<td>Pair 2</td>
<td>- -</td>
<td>48 48</td>
<td>100 100</td>
<td>41 44</td>
<td>7 7</td>
</tr>
<tr>
<td>Pair 3</td>
<td>- -</td>
<td>59 54</td>
<td>100 100</td>
<td>47 41</td>
<td>10 8</td>
</tr>
<tr>
<td>Pair 4</td>
<td>- -</td>
<td>62 59</td>
<td>95 100</td>
<td>21 34</td>
<td>38 5</td>
</tr>
<tr>
<td>Pair 5</td>
<td>- -</td>
<td>63 63</td>
<td>100 100</td>
<td>46 39</td>
<td>6 4</td>
</tr>
<tr>
<td>Pair 6</td>
<td>- -</td>
<td>64 64</td>
<td>100 100</td>
<td>44 30</td>
<td>3 6</td>
</tr>
<tr>
<td>Pair 7</td>
<td>- -</td>
<td>64 64</td>
<td>55 100</td>
<td>24 34</td>
<td>110 9</td>
</tr>
<tr>
<td>Pair 8</td>
<td>- -</td>
<td>68 67</td>
<td>100 100</td>
<td>44 39</td>
<td>29 7</td>
</tr>
<tr>
<td>Pair 9</td>
<td>- -</td>
<td>69 67</td>
<td>100 100</td>
<td>38 49</td>
<td>10 6</td>
</tr>
</tbody>
</table>

According to Wilcoxon’s test no statistically significant differences were found in the FAI (p = 0.59) and the BI (p = 0.12). However, there was a statistically
significant difference in discharge time (p = 0.04), indicating that neglect patients had a longer hospital stay than did patients without neglect.

*b) Anosognosia for illness*

Matched pairs were formed for patients who were unaware of stroke (anosognosic for illness) and those who were aware of stroke. The pairs were matched for visual neglect (BITC) and age. A maximum age difference of five years was allowed. Both subjects in the pair either had or did not have visual neglect. Five pairs were found (Table 17).

Table 17. Descriptive data of the matched pairs (anosognosia for stroke (A+) vs. intact awareness of stroke (A-)) in relation to age, visual neglect and the three functional outcome measures (the Barthel Index (BI), the Frenchay Activities Index (FAI) and discharge time in days) (N = 10)

<table>
<thead>
<tr>
<th>Matched pairs</th>
<th>Neglect</th>
<th>Age</th>
<th>BI score</th>
<th>FAI score</th>
<th>Discharge time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A+</td>
<td>A-</td>
<td>A+</td>
<td>A-</td>
<td>A+</td>
</tr>
<tr>
<td>Pair 1</td>
<td>+</td>
<td>+</td>
<td>59</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>Pair 2</td>
<td>+</td>
<td>+</td>
<td>61</td>
<td>57</td>
<td>85</td>
</tr>
<tr>
<td>Pair 3</td>
<td>+</td>
<td>+</td>
<td>62</td>
<td>63</td>
<td>20</td>
</tr>
<tr>
<td>Pair 4</td>
<td>+</td>
<td>+</td>
<td>64</td>
<td>64</td>
<td>95</td>
</tr>
<tr>
<td>Pair 5</td>
<td>+</td>
<td>+</td>
<td>72</td>
<td>69</td>
<td>55</td>
</tr>
</tbody>
</table>

According to Wilcoxon’s test no statistically significant differences were found in relation to the BI (p = 0.22) or the FAI (p = 0.23). There was a trend (p = 0.08) towards longer hospital stay in patients with anosognosia for illness as compared to those who were aware of stroke.

*c) Anosognosia for neglect*

Four matched pairs were found when the independent effect of anosognosia for neglect was examined. Matching was done for hemiparesis and age (maximum difference of five years). The data are described in Table 18.
Table 18. Descriptive data of the matched pairs (anosognosia for neglect (A+) vs. intact awareness of neglect (A-)) in relation to age, hemiparesis and the three functional outcome measures (the Barthel Index (BI), the Frenchay Activities Index (FAI) and discharge time in days) (N = 8)

<table>
<thead>
<tr>
<th>Matched pairs</th>
<th>Hemiparesis</th>
<th>Age</th>
<th>BI score</th>
<th>FAI score</th>
<th>Discharge time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A+  A-</td>
<td>A+  A-</td>
<td>A+  A-</td>
<td>A+  A-</td>
<td>A+  A-</td>
</tr>
<tr>
<td>Pair 1</td>
<td>+  +</td>
<td>57  57</td>
<td>90  80</td>
<td>21  21</td>
<td>154  65</td>
</tr>
<tr>
<td>Pair 2</td>
<td>+  +</td>
<td>58  61</td>
<td>85  85</td>
<td>24  24</td>
<td>128  177</td>
</tr>
<tr>
<td>Pair 3</td>
<td>+  +</td>
<td>66  65</td>
<td>80  95</td>
<td>33  33</td>
<td>102  67</td>
</tr>
<tr>
<td>Pair 4</td>
<td>-  -</td>
<td>62  63</td>
<td>95  100</td>
<td>21  21</td>
<td>38  6</td>
</tr>
</tbody>
</table>

Using the Wilcoxon’s test no statistically significant differences were found in the BI (p = 0.59), the FAI (p = 0.72) or discharge time (p = 0.47).

d) Anosognosia for hemiparesis

It was not possible to examine in detail the independent effect of anosognosia for hemiparesis in relation to the functional outcome measures, since only two matched (for visual neglect and age) pairs were found.

On the basis of these analyses of matched pairs, visual neglect had an independent effect on one outcome measure, namely discharge to home. The patients with visual neglect were hospitalised longer periods than patients without visual neglect. Patients with anosognosia for illness also had a tendency to stay in hospital longer than those who were aware of their illness. Anosognosia for neglect had no independent effect on the three outcome measures used.
6. DISCUSSION

6.1. Assessment of acute neglect

Double dissociations between the six conventional subtests of the BIT indicate that visual neglect is a heterogenous syndrome. For clinical purposes visual neglect defined by these tests can be measured as a unidimensional impairment. At the acute phase of stroke a combination of three tests provides an adequate evaluation of visual neglect: Line crossing, Letter cancellation and Line bisection subtests of the BIT.

This study confirmed the previous result by Halligan et al. (1989) that the BIT subtests measure some aspects of the same underlying construct, i.e. visual neglect. Halligan and others (1989) studied convalescent left or right hemisphere stroke patients and defined neglect as a performance below the cutoff score of 130 for the sum of the six BIT subtest scores (max. 146), based on data for 50 age-matched controls. The criteria for neglect in this study was failure in at least two of the six BIT subtests, using the same cutoff points for each subtest as Halligan et al. (1989). The double dissociations confirm that visual neglect is a heterogenous syndrome, which forms a weak clinical syndrome, but not a strong functional one, as reported earlier by Stone et al. (1998). Although it is now evident that neglect is not a unitary syndrome but a heterogenous combination of dissociating defects (Stone et al. 1998), the two studies demonstrate that for clinical purposes visual neglect could be measured with the conventional tests as a unidimensional impairment.

As indicated by Halligan and collaborators (1989) the BIT subtests have differing sensitivities, which was clearly confirmed by the present study. In both studies (Halligan et al. 1989; Study I) the best single BIT subtest for detecting neglect was Star cancellation. However, in the present study the sensitivity of Star cancellation was not very good (80%) and the test misdiagnosed seven cases. When the combination of Line crossing, Letter cancellation and Line bisection was used, only one neglect patient and one non-neglect patient remained unidentified.

The 15 subtests of the original BIT take about an hour to complete, and even the modified, seven-test version for right hemisphere stroke patients (Stone et al. 1991a, b) is not necessarily suitable for all acute stroke patients because of their poor condition and fatigue. Therefore, the three BIT subtests are recommended as bedside screening tests on acute stroke wards, where patients tire easily and cannot yet be examined with more extensive test batteries. For staff members information on possible visual neglect is useful even at the acute phase when helping these patients with everyday activities.

However, it should be noted that the same subtests may not be useful for evaluating visual neglect in chronic stroke patients. The assessment of a stroke patient’s ability to drive or return to work, for instance, requires different combinations of tests depending on whether that patient is in the early or later phase of stroke.
6.2. Dissociations of anosognosias in acute stroke

The present study discovered double dissociations of anosognosias for neglect and unawareness of illness, as well as anosognosia for neglect and anosognosia for hemiparesis. Furthermore, a simple dissociation was found between unawareness of illness and anosognosia for hemiparesis.

Previous studies (McGlynn and Schacter 1989; Bisiach and Geminiani 1991; Bisiach et al. 1986) indicate that anosognosia is not a unitary phenomenon resulting in poor awareness of most or all co-occurring deficits. However, these conclusions are based on findings of simple dissociations in group studies or observations on individual patients (Bisiach et al. 1986; Bakchine et al. 1997). The double dissociations of anosognosias found in the present consecutive series of right hemisphere stroke patients demonstrate that anosognosias for different defects are independent and specific impairments of awareness. Consequently, different anosognosias may have quite different effects on functional recovery.

In the present study, only verbal awareness (Diller and Riley 1993) of deficits (stroke, hemiparesis and neglect) was measured. Previously Berti et al. (1996) have reported a double dissociation between anosognosia for motor impairment and anosognosia for drawing neglect. Anderson and Tranel (1989) included in their Awareness Interview one question (“Are you having any trouble with your vision?”) concerning awareness of perceptual problems, but this question was not analysed separately. McGlynn and Schacter (1989) suggested that “the very existence of neglect could be construed as a form of anosognosia, inasmuch as unawareness (of the perceptual world) is a defining characteristic of the syndrome”. As previously reported by Halligan and Marshall (1998b), many neglect patients have conceptual and experiential insight into their deficit and its consequences. Thus, unawareness is not always a necessary component of visual neglect.

It may, of course, be questioned whether anosognosia for neglect can be measured with the single question (“Do you have any difficulties observing any part of the space?”) used in the present study, since a patient could vary in his or her response. However, this question reflects the stage of verbal or explicit awareness of neglect, just as the questions by Bisiach and others (1986) concerning anosognosias reveal how adequately the patient acknowledges his/her hemianopia or hemiparesis.

6.3. Predictors of functional outcome at one year after right hemisphere stroke

Acute visual neglect was one of the best single predictors of poor functional recovery according to all three outcome measures applied in the present study: 1) a standardised outcome measure, the Barthel Index, 2) the patient’s self-evaluated outcome, the FAI, and 3) time from stroke to discharge to home. However, the three outcome measures were partly predicted by different factors. Unawareness of illness was related to a longer hospital stay, but the other forms of anosognosias did not have an independent effect on the outcome measures.
In the present study functional outcome was evaluated with a homogenous group of patients with right hemisphere infarction. The best combination of predictors for an objective measure of functional outcome, the Barthel Index (BI), was hemiparesis and visual neglect (BITC) or visual neglect alone (BITB) in this group sample. The self-evaluated functional capacity (the FAI; Study II) was best predicted by BITB and age, while hemiparesis, unawareness of illness and presence of a relative at home were the best predictors for the time from stroke to discharge to home (Study IV). The differences in the predictors for the three outcome measures probably reflected the differences in the skills and abilities required by these outcome measures.

The BI is probably the best-known standardised ADL index used worldwide, but it covers only basic ADL functions. Since the BI heavily emphasises motor functions, it is not surprising that hemiparesis was one of the most significant predictors of poor outcome measured with the BI. The two other functional outcome measures, i.e. self-evaluated FAI and discharge to home, are probably more subjective in nature. The decision to discharge a patient from the rehabilitation ward is made by a multidisciplinary team when it is convinced that this patient will be able to cope at home. This decision is, of course, based on a variety of clinical and non-clinical reasons. Nevertheless, in Study IV, motor functioning was apparently emphasised in these decisions, too, since hemiparesis was the strongest predictor of poor recovery. Anosognosia for hemiparesis or anosognosia for neglect had no additional predictive value for the time from stroke to discharge to home.

Numerous studies (e.g. Kinsella and Ford 1980 and 1985; Denes et al. 1982; Kotila et al. 1986; Fullerton et al. 1986 and 1988; Paolucci et al. 1996a; Paolucci et al. 1998) lend support to the importance of visual neglect as an indicator of poor functional recovery in long-term follow-up. By contrast there are only a few studies that stress the importance of anosognosia as a predictor of functional outcome – although it has to be said that not very many studies have used anosognosias as predictors of recovery. Gialanella and Mattioli (1992) conducted their study with a homogenous group of right hemisphere patients with left hemiplegia one month after the onset of stroke. Anosognosia for hemiplegia emerged as a strong predictor of poor functional outcome. Since the outcome measure emphasised motor functions, it is reasonable to assume that anosognosia for hemiparesis predominantly hindered motor recovery. Other neuropsychological disorders were not considered. It is possible that the nine anosognosic patients had more serious general cognitive dysfunctions, e.g. worse memory or orientation, than the patients who were aware of their hemiplegia. Two studies by Pedersen et al. (1996, 1997) also suggest that anosognosia has an independent value in the prediction of functional outcome. Their outcome measure, the BI, also stresses motor functioning, and the two forms of anosognosia (for hemiparesis and for hemianopia) were not analysed separately. Their study group included right and left hemisphere stroke patients, and visual neglect was evaluated with a single test. The present study lends partial support to their result: unawareness of illness was related to a longer hospital stay, thus indicating poor functional recovery. In the present study, anosognosias for hemiparesis and unawareness of illness recovered within three months. This result suggests that acute anosognosias, especially
unawareness of illness, are associated with more persistent cognitive disorders that hinder recovery.

To summarise, functional recovery after stroke has been evaluated in mixed or heterogenous groups including patients with left and right hemisphere haemorrhagic or ischaemic stroke (e.g. Kinsella and Ford 1980 and 1985; Denes et al. 1982; Kotila et al. 1986). This means there may be plenty of confounding factors affecting the outcome. The time intervals from stroke to the first neuropsychological examination and follow-up examinations differ markedly between the studies. In many studies visual neglect has been evaluated with a single test, and anosognosia has usually been assessed only in relation to hemiparesis or hemianopia following the method of Bisiach et al. (1986) (Denes et al. 1982; Fullerton et al. 1986 and 1988; Gialanella and Mattioli 1992; Blanc-Garin 1994; Pedersen et al. 1997). The predictors used in outcome studies usually show strong intercorrelations. It is therefore difficult to define the independent impact of a single predictor in a heterogenous group of stroke patients unless these associations are carefully taken into account. Anosognosias are by definition associated with other deficits, for instance with hemianopia, hemiparesis or neglect, and it is difficult to differentiate the contribution of a single deficit to the outcome.

Many functional outcome measures emphasise motor functioning instead of social and cognitive abilities. The evaluation of outcome after right brain damage imposes special demands on an outcome measure. There is a lack of outcome measures that take into account the specific features of cognitive disorders and their impact on everyday functioning after right brain damage. The questionnaire by Towle and Lincoln (1991) and the Catherine Bergego Scale (Azouvi et al. 1996) were designed to detect the specific problems experienced by patients with visual neglect in everyday life, but they have not yet been widely adopted.

6.4. Clinical applications and possible implications for the future

Based on the results of Study I the three BITC subtests, Line crossing, Letter cancellation and Line bisection, are suggested for routine use in clinical practice to evaluate acute visual neglect. Visual neglect needs to be evaluated even in the acute stage of stroke because it has important implications for the patient’s longer term recovery. In this study, most patients with acute neglect became aware of it before the three-month follow-up examination and were able to compensate the defect in the repeated assessment with the BIT. Nevertheless, the prognostic significance of acute neglect suggests that after its partial recovery, it might still hamper overall functional recovery. It is undetectable in repeated situations, but might be harmful in novel circumstances. More sensitive tests are needed to detect mild recovering neglect.

Moreover, the evaluation of anosognosias appears to be useful for prognostic purposes in acute stroke. There is a general need to develop better methods for the assessment of anosognosia and a special need to take into account various forms of unawareness of deficits. The dissociation of verbal or explicit and behavioural or implicit awareness is a well-known phenomenon from case descriptions (McGlynn and Schacter 1989; Diller and Riley 1993; Robertson and Halligan 1999). For instance, a
hemiplegic patient may verbally acknowledge the defect, but repeatedly attempt to rise from bed and fall down, thus showing explicit awareness but implicit anosognosia for hemiplegia. There are no established methods for the assessment of behavioural or implicit forms of anosognosia. For instance, neglect patients usually learn to avoid circumstances that cause them harm, but they also have to restrict their activities, which results in incomplete and unsatisfactory overall functional recovery. They seem to be implicitly aware of the defect, but might verbally claim that they no longer have neglect. However, this latent neglect may be dangerous in novel situations, especially on the road. It is important then that the development of sensitive neglect tests and indicators of awareness of this defect goes hand in hand with the improvement of counselling, rehabilitation and prognosis of neglect patients.
7. CONCLUSIONS

1. Visual neglect was optimally detected in the acute phase with three conventional subtests of the BIT, namely Line crossing, Letter cancellation and Line bisection in this group sample. These tests can be performed as bedside screening tests in acute stroke because they are quick and easy to administer.

2. Double dissociations between the conventional subtests of the BIT indicate that visual neglect is a product of different mechanisms, but since its main components associate, the syndrome shares a common description, and can be reliably used for purposes of clinical assessment.

3. The double dissociation of anosognosia for neglect and anosognosia for hemiparesis as well as the double dissociation of anosognosia for neglect and unawareness of illness in a consecutive series of patients with right hemisphere infarct demonstrate that there are different and to some extent independent anosognosias for different defects. It would appear then that anosognosia is not a unitary phenomenon, but this finding does not exclude the possibility of a generalised unawareness of deficits. Furthermore, it should be taken into account that in the present study only verbal anosognosia was examined, and the measures used may have limitations.

4. Visual neglect in acute stroke is an important predictor of poor functional recovery in ADL. In this study, visual neglect and hemiparesis were associated with poor functional outcome during a one-year follow-up, when the outcome was evaluated by a neurologist using the standardised Barthel Index.

5. Visual neglect and age were associated with poor functional outcome during a one-year follow-up, when the outcome was evaluated by the patients themselves using an extended ADL scale, the Frenchay Activities Index.

6. Return to home during a one-year follow-up can be predicted with three indices: hemiparesis and unawareness of illness increased the duration of the hospital stay, and the presence of a relative at home reduced it. Visual neglect had predictive value only as a single variable. This indicates that motor functioning is the most important predictor of patients’ discharge to home after right hemisphere stroke.

7. Visual neglect and different forms of anosognosias should be evaluated in the acute phase, because these defects seem to be of importance in the prediction of long-term functional recovery.
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Mervi Jehkonen
9. REFERENCES


ORIGINAL PUBLICATIONS I – IV