

**SPONTANEOUS RECOVERY FROM VISUAL INATTENTION 12 MONTHS AFTER
RIGHT HEMISPHERE STROKE**

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ABSTRACT

Visual inattention is a frequent neuropsychological disorder after right hemisphere (RH) stroke and is known to have a negative impact on functional abilities of patients. Visual inattention is related to both lateralized attentional deficits and non-lateralized difficulties in visual processing. The aim of this thesis was to study spontaneous recovery from visual inattention during a 12-month follow-up focusing on visual reasoning abilities, visual reasoning speed, and initial rightward bias.

The study group consisted of 25 patients who were admitted to Tampere University Hospital due to a first-ever RH stroke. The presence of visual inattention was examined using the Behavioral Inattention Test (BIT) and the starting point (SP) analysis of its three cancellation tasks. Based on the results patients were divided into two groups and their SPs were measured along with those of a healthy control group (HC). Sixteen patients (64%) exhibited visual inattention (the VIN+ group) and nine (36%) did not (the VIN- group). Visual reasoning abilities were assessed using the Picture Completion task from the Wechsler Adult Intelligence Scale Revised (WAIS-R). At 12 months, laterality of the stimuli and the performance time on the first 12 items were also taken into account.

Results showed that the VIN+ group performed poorer than the VIN- group in the visual reasoning task in the acute phase. Their performances improved during the first six months after stroke so that at six and 12 months there were no differences between the patient groups. The visual reasoning performance of the VIN- group did not change during the follow-up period. When the performances of the patients were compared to the HC's, the number of patients performing within normal range was higher in the VIN- group at each examination. During the acute phase there were significant differences between the SPs of the groups in the cancellation tasks. The VIN+ group showed pathological SPs located on the right side that shifted towards the left during the first six months after stroke. There were no differences in SPs between the patient groups at six or 12 months. When visual reasoning speed was measured one year after stroke, the VIN+ group spent significantly more time finding the left-sided than the right-sided stimuli.

The VIN+ group showed spontaneous recovery from visual inattention during the first six months after stroke. Their visual reasoning abilities improved and the initial rightward bias decreased. However, visual inattention in the acute phase had long-standing effects: The VIN+ group exhibited slow visual processing on the left-sided stimuli even 12 months after stroke. In order to detect visual inattention and start rehabilitation in optimal time, this study suggests that the SP analysis should be used as a standard procedure along the conventional tests when assessing the presence of visual neglect and visual inattention.

Key words: Behavioral Inattention Test, neglect, starting point, visual inattention, visual reasoning speed

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TIIVISTELMÄ

Visuaalinen inattentio on yleinen neuropsykologinen häiriö erityisesti oikean aivopuoliskon infarktin jälkeen, ja sen on todettu heikentävän merkittävästi potilaiden toimintakykyä. Häiriöön liittyy sekä toispuolisia tarkkaavuuden suuntaamisen että yleistyneitä visuaalisen prosessoinnin vaikeuksia. Tämän tutkimuksen tarkoituksena oli tutkia visuaalisen inattentionin ilmenemistä ja spontaania kuntoutumista 12 kuukauden seuranta-aikana tarkkaavuuden suuntautumisen ja visuaalisen päättelysuoriutumisen, erityisesti päättelyn nopeuden, osalta.

Tutkimukseen osallistui 25 oikean aivopuoliskon infarktiin sairastunutta potilasta, jotka olivat olleet hoidettavina Tampereen yliopistollisen sairaalan neurologian akuuttiosastolla ensimmäisen aivoinfarktinsa vuoksi. Tutkittavien visuaalisen inattentionin ilmenemistä tutkittiin Behavioral Inattention Testillä (BIT) sekä sen etsintätehtävien aloituspisteanalysilla, joiden tulosten perusteella tutkittavat jaettiin kahteen ryhmään. Potilaiden ja terveiden verrokkien aloituspisteet mitattiin. Yhteensä 16:lla (64 %) potilaalla oli visuaalinen inattentio (VIN+ -ryhmä) ja yhdeksällä (36 %) ei ollut (VIN- -ryhmä). Visuaalisen päättelyn tasoa arvioitiin Wechsler Adult Intelligence Scale Revisedin (WAIS-R) kuvientäydennystehtävällä akuuttivaiheessa sekä kuuden ja 12 kuukauden seurantatutkimuksissa. Kahdentoista kuukauden seurantatutkimuksessa myös ärsykkeiden puoleisuus ja 12 ensimmäisen osatehtävän ratkaisemiseen käytetty aika otettiin huomioon.

Tulokset osoittivat, että VIN+ -ryhmän potilaat suoriutuivat akuuttivaiheessa muita potilaita heikommin visuaalisen päättelyn tehtävässä. VIN+ -ryhmän suoriutuminen parani kuitenkin ensimmäisen kuuden kuukauden aikana niin, että kuuden ja 12 kuukauden kontrollitutkimuksissa potilasryhmien suoriutumisessa ei enää havaittu eroja. VIN- -ryhmässä ei havaittu visuaalisen päättelyn muutoksia seuranta-aikana. Kun potilaiden suoriutumista verrattiin väestön keskiarvoon, normaaliin keskitasoon sijoittuvien suoritusten määrä oli kaikkina seuranta-ajankohtina selvästi suurempi niillä potilailla, joilla ei ollut visuaalista inattentiota akuuttivaiheessa. Etsintätehtävien aloituspisteissä havaittiin akuuttivaiheessa merkitseviä eroja potilasryhmien välillä. VIN+ -ryhmän poikkeavat aloituspisteet siirtyivät oikealta puolelta vasemmalle ensimmäisen kuuden kuukauden aikana. Kontrollitutkimuksissa ei havaittu tilastollisesti merkitseviä eroja aloituspisteissä potilasryhmien välillä. Kun visuaalisen päättelyn nopeutta analysoitiin vuosi aivoinfarktin jälkeen, havaittiin, että VIN+ -ryhmä käytti merkittävästi enemmän aikaa vasemmanpuoleisten kuin oikeanpuoleisten ärsykkeiden löytämiseen.

VIN+ -ryhmän visuaalisen inattentionin spontaani kuntoutuminen ilmeni visuaalisen päättelysuoriutumisen paranemisena ja poikkeavien aloituspisteiden siirtymisenä kohti terveiden verrokkien aloituspisteitä ensimmäisen kuuden kuukauden aikana aivoinfarktin jälkeen. Akuuttivaiheen visuaalisella inattentiolla oli kuitenkin pitkäaikaisia seurauksia: VIN+ -ryhmällä ärsyksen vasemmanpuoleinen sijainti hidasti visuaalista päättelyä vielä 12 kuukautta aivoinfarktiin sairastumisen jälkeen. Jotta visuaalinen inattentio tulisi ilmi ja kuntoutus voitaisiin aloittaa optimaaliseen aikaan, aloituspisteanalyysi tulisi ottaa osaksi neuropsykologista tutkimusta aina kun visuaalisen huomiotta jäämishäiriön tai visuaalisen inattentionin esiintymistä arvioidaan.

Avainsanat: aloituspiste, Behavioral Inattention Test, neglect, visuaalinen inattentio, visuaalisen päättelyn nopeus

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1. INTRODUCTION

1.1. Stroke

Stroke is a current issue: It is a major cause of long-term disability and death worldwide and one of the most prominent causes of death in Finland (Aivoinfarktin Käypä hoito -suositus, 2011; Feigin, Lawes, Bennett, Barker-Collo, & Parag, 2009). Although the annual number of incident stroke patients in Finland has decreased during the last two decades, the figure is still over 10 000 (Meretoja, Roine, Kaste, Linna, Juntunen, Erilä et al., 2010). Every quarter of stroke patients is of working age (Aivoinfarktin Käypä hoito -suositus, 2011). Stroke places a tremendous burden on health services: The estimated treatment costs nationwide are 1.1 billion euros.

In high-income countries there has been a 42% decrease in stroke incidence during the past four decades while in low- to middle-income countries stroke incidence has increased more than 100%, becoming an epidemic (Feigin et al., 2009). Since it has been shown that stroke is strongly related to unhealthy lifestyle and thus could often be prevented, the differences in incidence rates worldwide might reflect the local levels of detection and modification of risk factors. Some risks, like aging, gender, socio-economic status, and heredity, are challenging to control but there are also risks that are modifiable such as hypertension, diabetes, cardiovascular disease, hyperlipidemia, smoking, physical inactivity, and alcohol abuse (Benson & Sacco, 2000; Roger, Go, Lloyd-Jones, Benjamin, Berry, Borden et al., 2012).

Stroke is due to a disturbance in the blood supply to the brain caused by ischemia or hemorrhage (Roger et al., 2012). Intracerebral hemorrhage occurs within the brain tissue and subarachnoid hemorrhage is bleeding into the subarachnoid cavity. Approximately 80% of strokes are ischemic in origin. Ischemia occurs when vascular blockage reduces cerebral blood flow to tissues and prevents adequate delivery of oxygen and glucose (Aivoinfarktin Käypä hoito -suositus, 2011; Roger et al., 2012). The blockage can occur due to thrombosis, embolism, or systemic hypoperfusion (Feigin et al., 2009). Ischemic stroke causes the largest loss of quality-adjusted life years (Aivoinfarktin Käypä hoito -suositus, 2011; Feigin et al., 2009). Transient ischemic attack (TIA) occurs when the blood supply to the brain is blocked for a short time. TIA causes only temporary brain dysfunctions but is related to a highly elevated risk of stroke within the following three months (Johnston, Gress, Browner, & Sidney, 2000). Symptoms related to stroke appear unexpectedly and culminate fast (Aivoinfarktin Käypä hoito -suositus, 2011; Roger et al., 2012). Unilateral numbness on the limbs or

face, loss of balance and, depending on the side of the lesion, difficulties in language (left) or impaired spatial perception (right) are the first signs of stroke. Motor symptoms typically appear on the contralesional half of the body. Rapid treatment in a specialized stroke unit improves the prognosis significantly (Aivoinfarktin Käypä hoito -suositus, 2011; Marler, Tilley, Lu, Brott, Lyden, Grotta et al., 2000).

1.2. Cognitive impairments after stroke

Various cognitive impairments are typical consequences of stroke (Hochstenbach, Mulder, van Limbeek, Donders, & Schoonderwalt, 1998; Nys, Van Zandvoort, De Kort, Jansen, De Haan, & Kappelle, 2007; Tatemichi, Desmond, Stern, Paik, Sano, & Bagiella, 1994). According to Hochstenbach et al. (1998), more than 70% of stroke patients show slow information processing and over 40% have difficulties with memory functions, visuospatial and visuoconstructive functions, and language skills. Tatemichi et al. (1994) assessed stroke patients 60 years of age or older three months post-stroke and reported deficits involving attention, visuospatial ability, abstract reasoning, memory, orientation and language. Every third patient was classified cognitively impaired using a cut-off of failing in four or more items out of 17.

Cognitive impairments following cortical stroke depend on the laterality of the ischemia (Aivoinfarktin Käypä hoito -suositus, 2011; Nys et al., 2007). Nys et al. (2007) suggested that disorders in executive functioning (39%) and visual perception/construction (38%) are the most common cognitive impairments after stroke. Left hemisphere stroke is commonly related to difficulties in language, executive functioning and verbal memory, while patients with right hemisphere stroke typically show impaired visuospatial and attentional functions (Nys et al., 2007; Jehkonen, Kettunen, Laihosalo, & Saunamäki, 2007). Attentional impairments may show especially when there are multiple stimuli or a time limit putting a strain on the performance (Taylor, 2003).

Studying cognitive dysfunctions after stroke is essential since it is known that they can strongly predict long-term cognitive and functional outcomes (Jehkonen, Laihosalo, & Kettunen, 2006a, 2006b; Nys, Van Zandvoort, De Kort, Van der Worp, Jansen, Algra et al., 2005). According to Nys et al. (2005) executive dysfunction and defective abstract reasoning predict long-term cognitive impairment after stroke. In their review, Jehkonen et al. (2006b) pointed out that the presence of neglect after right hemisphere stroke has a significant and independent negative impact on functional outcome. Cognitive dysfunctions are often long-standing and many patients must cope with them for the rest of their lives (Hochstenbach, Otter, & Mulder, 2003; Nys et al., 2005).

1.2.1. Visual neglect and visual inattention

Visual neglect is the most common neuropsychological disorder after right hemisphere (RH) stroke (Buxbaum, Ferraro, Veramonti, Farne, Whyte, Ladavas et al., 2004; Jehkonen et al., 2007; Nys et al., 2007; Parton, Malhotra, & Husain., 2004) and during the last 15 years there has been an increasing amount of research on its prevalence. Nys et al. (2007) suggested that 52% of RH patients show visual neglect in the acute phase. In a study by Cassidy, Lewis and Gray (1998) 40.9% of RH patients showed visuospatial neglect. According to Bowen, McKenna and Tallis (1999) the median reported prevalence of visual neglect after RH stroke was 43%. Individual differences including lesion volume and location, as well as the nature and timing of assessment, might explain the variation of rates of occurrence and recovery after stroke. Overall the reported occurrence rate of visual neglect in RH patients without thrombolytic treatment has varied from 13% to 82% (Bowen et al., 1999).

Neglect is an attentional disorder that is characterized by a patient's failure to respond, report, or orient to stimuli on his contralesional side, even if there is no motor or sensory loss (Bowen et al., 1999; Halligan, Cockburn, & Wilson, 1991; Robertson & Halligan, 1999). It can be multimodal involving visual, auditory, and somatosensory systems (Jehkonen et al., 2007). Motor neglect refers to apparent failure to use contralesional limbs or to reach out to that side (Parton et al., 2004). Also, representational imagery is often impaired in patients with neglect: In their classical study, Bisiach and Luzzatti (1978) found that when patients were asked to describe a familiar place from a certain standing point, left-sided details were often omitted. The same happened when patients were asked to describe the place from an opposite direction: Previously described details were left undescribed.

Neglect has various subtypes. It may be body-centred, in which case the patient fails to attend to the environment and stimuli located on the left side of his body midline, or object-centred, meaning that the left side of the object itself goes undetected regardless of the location in relation to the viewer (Buxbaum et al., 2004). Neglect can affect a patient's personal, peripersonal, or extrapersonal space (Robertson & Halligan, 1999). The classification is commonly used in clinical assessment. Personal space refers to the patient's body, peripersonal space is within arm's reach, and extrapersonal space farther than that. According to Buxbaum et al. (2004), peripersonal neglect is the most common type of neglect and affects 27% of RH patients. On the other hand, only 1% of RH patients suffered from pure personal neglect. Combinations of subtypes are common. Nijboer, ten Brink, Kouwenhoven and Visser-Meily (2014) studied behavioural consequences of peripersonal or extrapersonal neglect, and found that patients with only peripersonal or both peripersonal and extrapersonal neglect were more impaired in daily tasks than patients with only extrapersonal neglect. Patients with only extrapersonal

neglect, on the other hand, had more difficulties in tasks related to finding a route. Nijboer et al. (2014) emphasize the importance of accurately distinguishing the type of region-specific neglect in order to come up with the most reasonable rehabilitation plan.

The degree of neglect varies from mild to severe, and is typically more severe in the acute phase after stroke (Robertson & Halligan, 1999). In their study on 204 patients with acute RH stroke Gottesman, Kleinman, Davis, Heidler-Gary, Newhart, Kannan et al. (2008) found that advanced age significantly increased the risk of severe neglect even when the size of the lesion and stroke severity were controlled. This may be caused by brain atrophy and weaker compensational abilities related to older age. Also, working memory deficits have been found to correlate with neglect severity (Husain & Rorden, 2003).

Neglect occurs when brain regions responsible for cognitive functions in attentional, coordinate, and spatial domains get impaired (Halligan, Fink, Marshall, & Vallar, 2003; Jehkonen et al., 2007). It is usually related to focal lesions on the cortical areas perfused by the right middle or posterior cerebral arteries but it has been associated with lesions on both cortical and subcortical areas (Mort, Malhotra, Mannan, Rorden, Pambakian, Kennard et al., 2003; Parton et al., 2004). In cortical areas, damages to the inferior parietal lobe, medial temporal lobe, frontal lobe, or cingulate gyrus may evoke neglect (Mort et al., 2003). The putamen, pulvinar, and nucleus caudatus – the subcortical structures on the right hemisphere that connect to cortical superior temporal gyrus – are typically associated with visual neglect (Karnath, Himmelbach & Rorden, 2002). Classically, neglect has been considered to occur after damage to the right parietal cortex, but further studies have suggested that more complex and widespread neural networks related to attention are involved (Mort et al., 2003). According to a common attentional theory the RH is responsible for dividing attention on both sides, whereas the left hemisphere is responsible only for the right side (Bowen et al., 1999). When the RH cannot function properly due to infarction, attention tends to unilaterally shift towards the right side. Imbalance in the visual attentional network causes the personal midline to shift to the right (Corbetta & Schulman, 2002).

Neglect after RH stroke has an independent impact on functional disability, high family burden, and low general attentional functions (Buxbaum et al., 2004). In their review, Jehkonen et al. (2007) describe the everyday challenges neglect patients face: Difficulties in dressing, shaving, eating, reading, and writing are very common. Since daily activities require adequate visual and spatial perception and the patient may be unaware of his disorder (anosognosia), neglect can be a disabling disorder challenging a patient's independence and functional outcome (Jehkonen, Laihosalo, & Kettunen, 2006a, 2006b; Robertson & Halligan, 1999).

1.2.2. Initial rightward bias and visual processing

Visual neglect is more frequent and severe than other forms of neglect (Gainotti, 2010), and it has drawn the most scientific interest (Robertson & Halligan, 1999). Two types of visual neglect can be observed: the lateralized type, exhibited as initial rightward bias and failure to orient to the contralesional side, and the non-lateralized type that shows slow visual processing and difficulties sustaining attention (Jehkonen et al., 2007). Initial rightward bias is displayed as a patient's tendency to start a visual search from the right since they experience difficulties estimating their body midline (Robertson & Halligan, 1999). It has clinical significance even without more severe visual neglect, and has been found to increase wheelchair accident risk (Webster, Roades, Morrill, Rapport, Abadee, Sowa et al., 1995): Patients easily collide into objects approaching them from the contralesional side and may act as if that side of the world has ceased to exist (Halligan & Marshall, 1998).

RH is known to be dominant for various attentional mechanisms (Robertson, 2001) and non-lateralized attentional deficits such as impaired visual reasoning, slow visual processing, and impaired sustained attention are often co-occurring (Jehkonen et al., 2007). Robertson, Mattingley, Rorden and Driver (1998) studied RH patients with left neglect eight and one-half months post-stroke and found that they became aware of left-sided visual stimulus more than half a second later than the right-sided one. Buxbaum et al. (2004) found that RH patients with neglect were more likely to suffer from non-lateralized symptoms than patients without neglect. The severity of these deficits is related to greater severity of neglect and they may exacerbate the lateralized symptoms, worsening the prognosis of recovery (Husain & Rorden, 2003; Robertson & Halligan, 1999). Viken, Samuelsson, Jern, Jood and Blomstrand (2012) compared stroke patients with lateralized or non-lateralized visual inattention and found that lateralized symptoms were more often associated with persistent visual inattention and severe neurological symptoms. According to their study, acute lateralized inattention predicted functional dependency especially after RH stroke. Recovery from lateralized neglect has been found to be associated with simultaneous improvement of non-lateralized impairments. However, non-lateralized symptoms may also occur separately in patients without neglect (Husain & Rorden, 2003).

Mild or residual visual neglect, namely visual inattention, is harder to detect but nonetheless complicates a patient's life significantly (Taylor, 2003). Initial rightward bias is a long-standing symptom of visual inattention that may not show in conventional tests since patients have learned to reorient their attention to the contralesional side (Jalas, Lindell, Brunila, Tenovuo, & Hämäläinen, 2002). Studies have shown that patients with visual inattention may perform well in structured and familiar environments but start to show rightward bias when facing more complex situations and tasks

(Taylor, 2003). Olk, Harvey and Gilchrist (2002) studied the saccadic eye movements of a patient who, according to the conventional measures, had recovered from visual neglect three months after stroke. They found that the patient still showed a strong initial rightward bias in visual multiple stimuli tasks. In a study by Kettunen, Nurmi, Dastidar and Jehkonen (2012), RH stroke patients who had suffered from visual neglect in the acute phase showed pathological starting points in visual search tasks six months post-stroke. The presence of initial ipsilesional bias may underlie the apparent recovery even 12 months after stroke (Mattingley, Bradshaw, Bradshaw, & Nettleton, 1994).

1.2.3. Assessing visual neglect and visual inattention

There are various methods to assess visual neglect. First of all, it is important to distinguish it from hemianopia, which is caused by damages to the visual cortex (Jehkonen et al., 2007). Azouvi, Samuel, Louis-Dreyfus, Bernati, Bartolomeo, Beis et al. (2002) have assessed the sensitivity of clinical and behavioural tests of spatial neglect after RH stroke and reported that behavioural assessment of neglect in daily life was more sensitive than any other single measure since the severe forms of neglect become apparent in the patient's behaviour. In severe cases a patient's head may be all together turned towards the ipsilesional side so detecting neglect is easy (Jehkonen et al., 2007).

A thorough neuropsychological examination is required in order to assess the severity of neglect and the possible cognitive impairments related to it. The lateralized impairments show not only in patients' everyday activities but also in visual search tasks (Husain & Rorden, 2003). Paper-and-pencil tests in peripersonal space are commonly used in assessing unilateral neglect and are adequate also for bedside testing (Robertson & Halligan, 1999). One of the most frequently used tests is the Behavioral Inattention Test (BIT; Jehkonen, 2002a; Wilson, Cockburn, & Halligan, 1987), found to be a reliable and valid standardized screening tool for assessing the presence of neglect. BIT consists of two types of tests: six conventional paper-and-pencil tests (BITC) and nine behavioural tests (BITB) that can be used separately in clinical settings. BITC includes three cancellation tasks (line, letter, and star cancellation), shape and figure copying, line bisection, and representational drawing. Figure 1 presents an example of a BIT figure copying performance of a patient with visual inattention seven days and six months post-stroke.

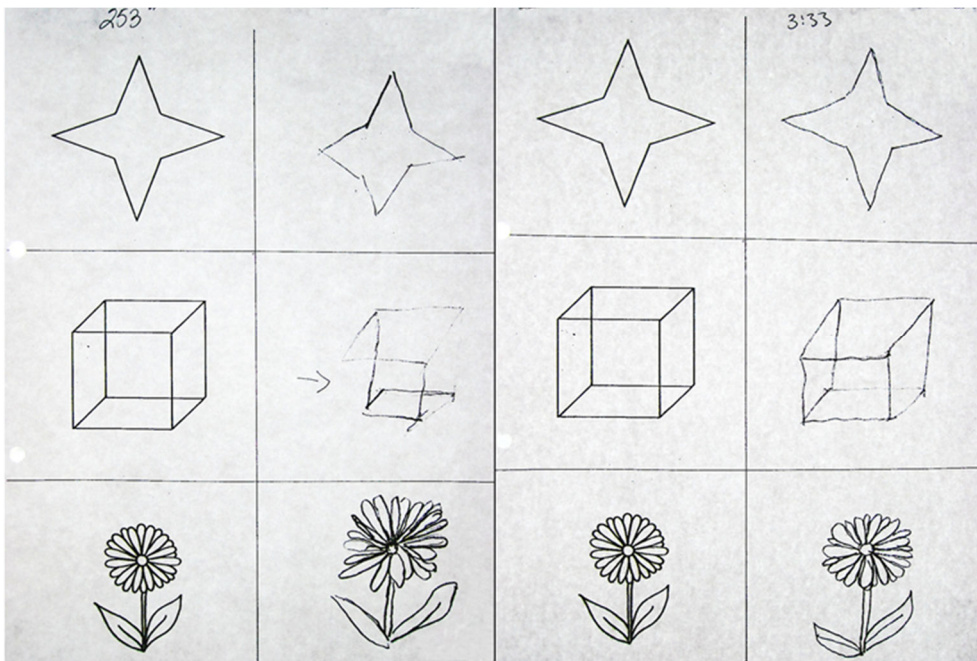


FIGURE 1. The BIT figure copying performance of a 74-year-old woman who had suffered an infarct on the area of the right middle cerebral artery. Seven days after stroke (left) she spent over four minutes on the task and missed some left-sided details. Six months after stroke (right) she spent 40 seconds less drawing the figures and completed them successfully.

Since administering the six subtests may be too tiresome for the patient, Jehkonen, Ahonen, Dastidar, Koivisto, Laippala and Vilkki (1998) suggested that a three-test combination of line cancellation, letter cancellation, and line bisection can be sufficient in detecting neglect in the acute phase. Cassidy, Lewis and Gray (1998) have suggested that poor line cancellation task performance in the acute phase is associated with a worse prognosis.

BIT is a valid and reliable test when assessing patients with moderate to severe forms of neglect, but it may not be sensitive enough to detect visual inattention (Jalas et al., 2002; Taylor, 2003). Due to compensation strategies the rightward bias may go undetected if situations and tasks are predictable or structured (Taylor, 2003). Initial rightward bias is common in patients with visual inattention (Jalas et al., 2002; Kettunen et al., 2012) and is the most sensitive clinical measure of neglect (Azouvi et al., 2002). According to Azouvi, Bartolomeo, Beis, Perennou, Pradat-Diehl and Rousseaux (2006), the most sensitive pencil-and-paper measure for RH stroke patients is the starting point (SP) location analysis in the BIT cancellation tasks. It has been suggested that approximately 80% of healthy controls (HC) tend to use a left-to-right scanning strategy, when the majority of RH stroke patients tend to do the opposite and start from the right (Azouvi et al., 2006). In the study by Kettunen et al. (2012), 71–100 % of HCs started cancellation tasks from the left.

In order to detect visual inattention Nurmi, Kettunen, Laihosalo, Ruuskanen, Koivisto and Jehkonen (2010) studied HCs and RH patients with and without neglect during the acute phase, analyzing the SPs of cancellation tasks and setting task-specific guideline values for clinical use. They concluded that starting one task outside the guideline value does not mean visual inattention since it can also be seen in HCs, but two or more SPs outside guideline values do indicate visual inattention. They found that one-third of the supposed non-neglect patients showed visual inattention. Line and star cancellation tasks were found to be especially sensitive tools in detecting it. Jalas et al. (2002) found that half the patients that did not have neglect according to conventional tests showed right-sided SPs in cancellation tasks.

Conventional methods alone are not always sensitive enough to detect visual inattention (Jalas et al., 2002), but combining them with SP analysis and reaction time tasks may increase the detection rate (Nurmi et al., 2010; van Kessel, van Nes, Brouwer, Geurts, & Fasotti, 2010). Visual inattention may also be noticeable in tests designed to assess other cognitive functions, especially if they contain horizontally placed stimuli (Lezak, 2004). Therefore tasks that require adequate visual reasoning speed or normal visual search abilities may bring visual inattention up, especially if the stimuli are laterally positioned. For example, performing successfully in the Picture Completion task of the Wechsler Adult Intelligence Scale Revised (WAIS-R) requires visual recognition of essential details of objects and adequate visual processing speed since there is a 20-second time limit allotted for each picture (Wechsler, 1981).

1.2.4. Spontaneous recovery from visual neglect and visual inattention

Follow-up studies have shown that spontaneous recovery from visual neglect is fairly common and occurs especially during the first two to six months after stroke (Appelros, Nydevik, Karlsson, Thorwalls, & Seiger, 2004; Jehkonen, 2002b). Jehkonen (2002b) reported that 57% of patients recover from neglect during the first three months after stroke. Recovery from lateralized symptoms such as rightward bias has been found to co-occur with recovery from non-lateralized symptoms like slow visual processing (Husain & Rorden, 2003). Figure 2 presents an example of the decrease of initial rightward bias in the star cancellation task, indicating spontaneous recovery six months after stroke.

Assessing recovery from visual inattention can be challenging since it may not show in conventional tests (Mattingley et al., 1994). Patients have often learned to use compensatory strategies in predictable and structured situations. Kettunen et al. (2012) studied RH patients' recovery

from neglect during a six-month follow-up. They found that although the BIT scores measuring neglect improved and thus indicated partial recovery from neglect, patients with acute phase neglect showed abnormal SPs in the cancellation tasks even six months post-stroke.

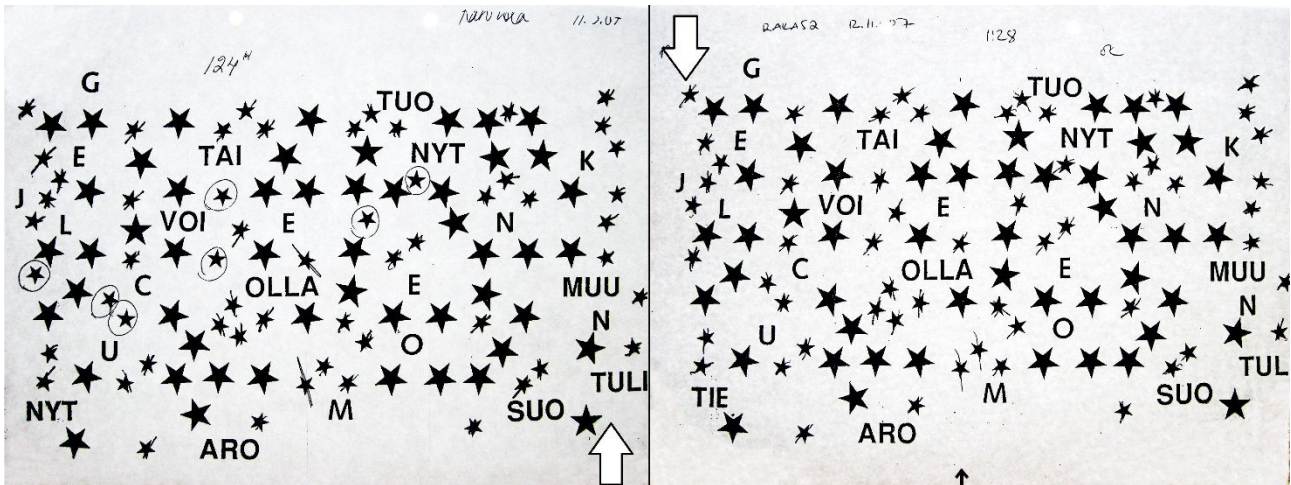


FIGURE 2. An example of an abnormal starting point (left) in the star cancellation task seven days after stroke. The patient started her search from the spot indicated by the white arrow showing a strong rightward bias. Circles around the stars point out the items she missed. Six months later (right) the SP is considered normal and the patient has found all the target items 36 seconds faster than in the original task. The patient was a 74-year old woman who had suffered an infarct on the area of the middle cerebral artery.

It is known that patients with visual inattention may perform well in simple tasks but show rightward attentional bias when facing more complex tasks (Lezak, 2004; Taylor, 2003). Distractions also put a strain on attentional functions (Robertson & Halligan, 1999). Robertson and Halligan (1999) described a condition which often becomes obvious after apparent recovery from visual inattention: Patients are first able to perceive stimulus—a picture, for example—on their contralesional side, but when this picture is presented simultaneously with another picture on the ipsilesional side, the patient notices only the ipsilesional one. If given enough time, patients with visual inattention might, for example, be able to find all the target stimuli on a task sheet, but if they are simultaneously exposed to competing stimuli, the contralesional space frame might again be left unattended (Schendel & Robertson, 2002). Therefore, it may be beneficial to combine conventional tests with time-limited tasks and SP analysis when assessing the recovery from visual inattention (Nurmi et al., 2010; van Kessel et al., 2010).

Cognitive dysfunctions following stroke are known to be long-standing and some patients will never fully recover (Hochstenbach, den Otter, & Mulder, 2003; Kerkhoff & Schenk, 2012). It has

been estimated that one-third of neglect patients will remain impaired (Kerckhoff & Schenk, 2012). Larger lesions, severe neglect and anosognosia at the baseline often predict persistent neglect (Jehkonen, 2007; Maguire & Ogden, 2002).

Functioning successfully and safely in everyday life –driving a car, for example – requires flexible shifting of attention and an ability to process complex visual stimuli (Taylor, 2003). These abilities are known to be impaired with visual inattention (Jalas et al., 2002). Initial rightward bias and slow visual processing related to visual inattention challenge patients' functional and working abilities and may increase the risk of accidents, e.g. in wheelchair maneuvering (Jehkonen et al., 2007; Webster et al., 1995). Many recent studies on visual inattention have focused on SP analysis, which has proven to be an adequate tool for assessing the presence of the condition (Azouvi et. al, 2006; Nurmi et al., 2010).

In this study, SP analysis is combined with a time-limited visual reasoning task, and in order to gain further information about the quality of performance one year after stroke, laterality of the stimuli and the visual processing time have been taken into account. This approach may bring up new information about visual inattention and the course of its spontaneous recovery.

1.3. Aims of the study

Research questions of this study were:

1. Do RH patients with left visual inattention differ from the other RH patients in visual reasoning in acute phase, at six months and 12 months after stroke?

Since it is well established that visual inattention is often related to difficulties processing visual stimuli (Jehkonen et al., 2007), it is assumed that patients with left visual inattention will perform poorer than other RH patients in the WAIS-R Picture Completion task. The Picture Completion task measures visual recognition and reasoning abilities that are often impaired after RH stroke (Lezak, 2004).

2. Do visual reasoning abilities of patients with visual inattention improve during the first year after stroke?

Studies have shown that at least partial recovery from neglect occurs spontaneously during the first six months after stroke (Appelros et al., 2004; Jehkonen, 2002b; Jehkonen et al., 2007). Jehkonen (2002b) found that 57% of patients recovered from visual neglect during the first three months after stroke. Recovery from non-lateralized symptoms often co-occurs with recovery from lateralized symptoms (Husain & Rorden, 2003). Studies with SP analyses have shown that initial rightward bias decreases during the first six months after stroke (Kettunen et al., 2012). Thus, it is expected that an improvement occurs in visual reasoning, as well.

3. Do patients with visual inattention need more time to find left-sided stimuli than right-sided stimuli 12 months after stroke?

Initial rightward bias is a prominent symptom of visual inattention (Jalas et al., 2002; Nurmi et al., 2010) and even with compensation strategies it may affect visual processing by slowing it down (van Kessel et al., 2010). According to Robertson et al. (1998), RH patients with left neglect became aware of left-sided visual stimuli more than half a second later than the right-sided ones, even 35 weeks after stroke. Combining the rightward bias with general slow speed, it is assumed that patients who suffered from visual inattention in the acute phase will perform more poorly and need more time to find the left-sided visual stimuli than the right-sided even 12 months after stroke.

4. Do SPs differ between the patients and the HCs, and do they change at the one-year follow-up?

SP analysis is the most sensitive pen-and-paper measure of visual inattention for RH patients (Azouvi et al., 2006). It has been suggested that approximately 80% of HCs tend to start visual search tasks from the left side of the sheet. The same percentage of RH patients with visual neglect show a tendency to use a right-to-left scanning strategy. Therefore, it is hypothesized that differences in the SPs between the groups will come up, especially in the acute phase when visual inattention related to stroke are known to be more frequent (Robertson & Halligan, 1999). Kettunen et al. (2012) studied the change in SPs of visual neglect patients at six months after stroke and found that both the presence of visual neglect and the magnitude of rightward bias changed over time: Rightward bias was nonetheless quite persistent and decreased significantly only in the line cancellation task. Therefore, it is assumed that the SPs of the patients with visual inattention will differ from the SPs of the HCs in the acute phase but during the follow-up period they will become more similar and move towards the left side.

2. METHODS

2.1. Subjects

The patient group consisted of 25 patients who were examined three times after they had been admitted in Tampere University Hospital due to a first-ever right hemisphere stroke. Overall 1458 consecutive patients between June 2005 and June 2008 were screened. The exclusion criteria ($n = 1433$) were: left hemisphere stroke ($n = 276$), TIA ($n = 200$), previous stroke ($n = 185$), age over 80 years ($n = 144$), cerebral hemorrhage ($n = 139$), other neurological diagnosis ($n = 137$), inability to participate in neuropsychological examination ($n = 95$), significant cerebral atrophy shown in computed tomography (CT) ($n = 92$), brain stem or cerebellar stroke ($n = 57$), substance abuse ($n = 21$), psychiatric disorder ($n = 20$), traumatic brain injury ($n = 6$), left-handedness ($n = 5$) and native language other than Finnish ($n = 4$). Also patients who were who did not participate in all three neuropsychological examinations, namely the acute phase, the six-month and the 12-month examinations ($n = 52$) were excluded. The study was approved by the Ethical Committee of Tampere University Hospital and an informed consent was obtained from all patients before attending the study. Neurological, neuroradiological and neuropsychological examinations were administered in

the acute phase as standard methods of treatment. The neuropsychological assessment was conducted on average three days after stroke.

HCs ($n = 50$) were volunteers, right-handed and aged between 30 and 80 years. They were recruited from local pensioners' clubs and from among the examiner's acquaintances. Exclusion criteria included previous or current neurological or psychiatric disorder. All HCs underwent a neuropsychological examination and were blind to the hypotheses of the study. The possible cognitive decline was evaluated by the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), where exclusion score was set to 24.

2.2. Neurological and neuroradiological examination

Stroke severity was assessed with the National Institutes of Health Stroke Scale (NIHSS; Goldstein, Bertels, & Davis, 1989). The degree of stroke was based on NIHSS sum score (range 0–34; 0 = no defect, 34 = severe stroke). Neuroradiological examination included magnetic resonance imaging (MRI) and CT. Neuroradiologist examined the results of MRI and CT and verified that the infarct was unilateral and was located on the right, and that there was no significant cerebral atrophy.

2.3. Neuropsychological examination

Neuropsychological assessments were conducted in the acute phase and at six and 12 months after stroke. In the acute phase the presence of visual neglect was assessed using the six conventional subtests of the BITC. Neglect was considered present if a patient scored at or below the cut-off level in at least two of the BITC subtests. The cut-off point was defined according to the test manual by Wilson, Cockburn and Halligan (1987). During each task the A4-sized task sheet was placed in front of the subject on a table and aligned with their body midline. In order to ensure the standard administration subjects were not allowed to move the sheets.

Three cancellation subtests were administered. In the line cancellation task the subject was instructed to find all 40 randomly spaced lines on a sheet and cross them over. Two central lines were crossed by the examiner as an example and the central lines were not scored (maximum score 36, cut-off 34). The letter cancellation task consists of 40 target letters (E and R) and 130 false targets (other letters) randomly scattered on the sheet. The subject was asked to mark all the target letters. Two additional letters under the stimulus rows were marked by the examiner as an example and were not scored (maximum score 40, cut-off 32). The star cancellation task includes 56 targets (small stars) and 75 false targets (big stars, words and letters) randomly spaced on a sheet. The subject was asked

to mark all the small stars. Two of the centred target stars were marked by the examiner as an example and were not scored (maximum score 54, cut-off 51).

In the figure and shape copying test the subject was first required to copy three drawings from the left side of the sheet. The drawings (a star, a cube and a flower) are arranged vertically and were clearly shown to the subject. In the second part of the test the subject was instructed to copy a group of three geometrical shapes presented on the left side of a separate sheet. The shapes were not pointed out to the subject. Scoring was based on the completeness of the drawings (maximum score 4, cut-off 3). In the line bisection task the subject was asked to estimate and indicate the midpoints of three horizontal lines placed in a staircase fashion across the sheet. Scoring of the test was based on the extent of deviation from the actual midpoints (maximum score 9, cut-off 7). In the representational drawing task the subject was asked to draw pictures of a clock face with numbers, a man or a woman, and a butterfly, on three separate sheets of blank paper. The task assesses the subject's visual imagery. Scoring was based on completeness of the drawings (maximum score 3, cut-off 2).

In order to distinguish the patients with left visual inattention from the others, SP analysis was conducted following the task-specific guideline values set by Nurmi et al. (2010). The SPs were determined in three BIT cancellation tasks by measuring the distance between the SP and the middle line of the stimulus sheet. The guideline values for normal SPs are -5.85 cm in the line cancellation task, -10.05 cm in the letter cancellation task and -11.05 cm in the star cancellation task. Beginning the task from the left side of the cut-off point is considered normal. Two SPs out of three on the right side of the cut-off points indicates pathological rightward bias and visual inattention. The SPs of the HCs were measured only once.

Patients' performances in the visual reasoning task were assessed using the WAIS-R Picture Completion task in three points of examination: in the acute phase, and again at six months and 12 months after stroke. Their task was to look at the pictures and tell what important part was missing. When comparing the overall performance at each examination sum scores were used. In order to find out the time spent on the stimuli at 12 months, only the first 12 pictures were included. These 12 pictures were chosen since all the patients had performed them and since half of them had stimulus on the left side and half in the middle or right. Thus, it became easier to compare the time spent on the stimuli on each side.

2.4. Data analysis

Nonparametric methods were chosen due to a small sample size and a skewed distribution on variables. Mann-Whitney U test was used to analyse the differences in continuous variables between the subject groups and chi square analysis was used to analyse nominal variables. Wilcoxon test was used to measure change in continuous variables between the three examination points. Comparisons between the two patient groups and the HCs were carried out using Kruskal-Wallis analysis of variance. Analyses were performed using the SPSS (Statistical Package for the Social Sciences) version 22.0 for Windows. For all analyses the level of statistical significance was set at .05.

3. RESULTS

The study group consisted of 13 males and 12 females. Patients were divided into two groups based on their performance in the BITC tasks. According to the BITC tasks only six patients suffered from visual neglect. However, when visual inattention was assessed using the SP analysis 10 more patients came up. Therefore, in the acute phase 16 patients (64%) suffered from left visual inattention or neglect (the VIN+ group) and nine (36%) did not (the VIN- group). Median age in the whole group was 62 (range: 31–78) and median years of education was 9.5 (range: 8–15). NIHSS score medians at baseline, in the acute phase and at six months were 4 (range: 1–17), 1 (range: 0–14) and 0 (range: 0–6), respectively. The VIN+ group had more severe strokes (NIHSS; $U = -2.733$; $p = .006$). Subject characteristics and their statistical significances are presented in more detail in Table 1.

The HC group ($n = 50$) consisted of 26 males and 24 females. Their median age was 60 (range: 30–80), median years of education 11 (range: 5–11) and median MMSE score 29 (range: 25–30). The HC group did not differ from the patient groups according to age ($\chi^2 (2) = 0,812$; $p = .666$), gender ($\chi^2 (2) = 0,317$; $p = .853$), or education ($\chi^2 (2) = 4,202$; $p = .122$).

3.1. Differences between patients with and without inattention in the visual reasoning task

Table 2 presents the medians and ranges of the Picture Completion sum points of the VIN+ and VIN- groups in the acute phase, at six months and 12 months after stroke. The groups differed from each other only in the acute phase: the VIN+ group's median raw score was 10 and VIN- group's median raw score was 16. In the other examinations there were no statistically significant differences between the patient groups.

TABLE 1. Characteristics of the VIN+ and VIN- groups and their statistical comparisons

Variable	VIN+ (n=16)	VIN- (n=9)	<i>p</i>
Male/Female	9/7	4/5	.571
Thrombolysis:yes/no	8/8	6/3	.420
Age: Md (range)	65.5 (31–78)	62 (57–76)	.910
Years of education: Md (range)	9.75 (8–15)	9 (8–14)	.774
Days from stroke onset to acute examination: Md (range)	3 (1–9)	3 (2–5)	.410
Days from stroke onset to 6 months examination: Md (range)	192 (180–258)	192 (185–222)	.658
Days from stroke onset to 12 months examination: Md (range)	375 (263–455)	439 (309–748)	.461
NIHSS in the baseline: Md (range)	4 (1–17)	4 (1–9)	.440
NIHSS in the acute phase: Md (range)	2.5 (0–14)	0 (0–4)	.006**
NIHSS at 6 months: Md (range)	0 (0–6)	0 (0–1)	.313
Hemianopia present in the baseline	27%	11%	.354
Hemianopia present in the acute phase	13%	0%	.279
Hemianopia present at 6 months	7%	0%	.480

VIN+ = visual inattention group; VIN- = non-inattention group; Md: median; NIHSS = National Institutes of Health Stroke Scale (range 0–34; 0 = no defect, 34 = severe stroke); ** = $p < .01$

TABLE 2. The medians and ranges of Picture Completion (PC) raw sum scores in the acute phase, at six and 12 months after stroke and their statistical comparisons between the VIN+ and VIN- groups.

PC raw scores	VIN+ (<i>n</i> =16)	VIN- (<i>n</i> =9)	U	<i>p</i>
Acute phase: Md (range)	10 (4–17)	16 (8–19)	-2.341	.019*
6 months: Md (range)	15 (8–19)	16 (10–21)	-.856	.392
12 months: Md (range)	15.5 (5–19)	17 (10–21)	-1.393	.164

VIN+ = visual inattention group; VIN- = non-inattention group; Md = median, * = $p < .05$

3.2. Spontaneous recovery of visual reasoning

Data analysis showed Picture Completion raw scores improving in the VIN+ group from the acute phase to six months. The change in the scores of the VIN- group was not significant. From six months to 12 months there were no changes in the sum scores for neither of the groups. Table 3 presents the statistical significance of change in scores between the three examinations.

TABLE 3. Statistical significance of improvement in Picture Completion task performance.

Group	Acute to 6 months		6 months to 12 months	
	Z	<i>p</i>	Z	<i>p</i>
VIN+	-3.305	.001***	-.045	.964
VIN-	-.955	.339	-.351	.726

VIN+ = visual inattention group; VIN- = non-inattention group, *** = $p < .001$

Raw sum scores were converted into standard scores in order to compare the patient groups' performance to the performance of the HCs based on the WAIS-R handbook (Wechsler, 1981). Table 4 presents the VIN+ and VIN- groups' division into performance groups based on whether their standard scores were

- a) 8 or more (mild decline or normal performance in visual reasoning)
- b) 4–7 (moderate decline)
- c) 3 or less (severe decline)

In the acute phase performances by the VIN+ group were quite evenly divided between the three groups. One-third (31.3%) of the patients performed within normal range or showed only mild decline, one-third (31.3%) of performances were moderately declined, and 37.5% were severely declined. At six months half the VIN+ patients performed within average performance limits and one third showed moderate decline of performance. At 12 months still 37.6% of the VIN+ patients performed poorer than average, a half showing moderate and a half severe decline.

In the acute phase two-thirds of the VIN- patients reached the average performance limits. Every tenth performance was in the lowest performance group indicating severe decline. At six months 77.8% of the VIN- patients performed within the average range and the rest were moderately declined. At 12 months only 11.1% of VIN- performances were moderately below average level and the rest were within normal range.

TABLE 4. The VIN+ and VIN- groups' performance in Picture Completion task compared to the HCs in the acute phase, at six months and 12 months.

Time of examination	Mild decline or normal	Moderate decline	Severe decline
I Acute phase			
VIN+	31.3%	31.3%	37.5%
VIN-	66.7%	22.2%	11.1%
II Six months			
VIN+ ¹	50%	31.3%	6.3%
VIN-	77.8%	22.2%	-
III 12 months			
VIN+	62.5%	18.8%	18.8%
VIN-	88.9%	11.1%	-

VIN+ = visual inattention group; VIN- = non-inattention group; ¹ Data for two subjects missing; SD = standard deviation

Figure 3 presents the median standard scores of the patient groups in relation to the performance levels in three examinations. Scores above 8 indicate only mild decline or normal performance, scores between 4 and 7 indicate moderate decline and scores below 4 severe decline in visual reasoning, while 10 is the normal average. The Figure 3 shows that in the acute phase the scores of the VIN+ group (4) were significantly lower than the scores of the VIN- group (9) indicating a moderate to severe decline, but they increased during the first six months after stroke and reached the low average performance level (8). The median standard scores of the VIN- group were placed within the normal variation throughout the follow-up period and did not change significantly between the examinations.

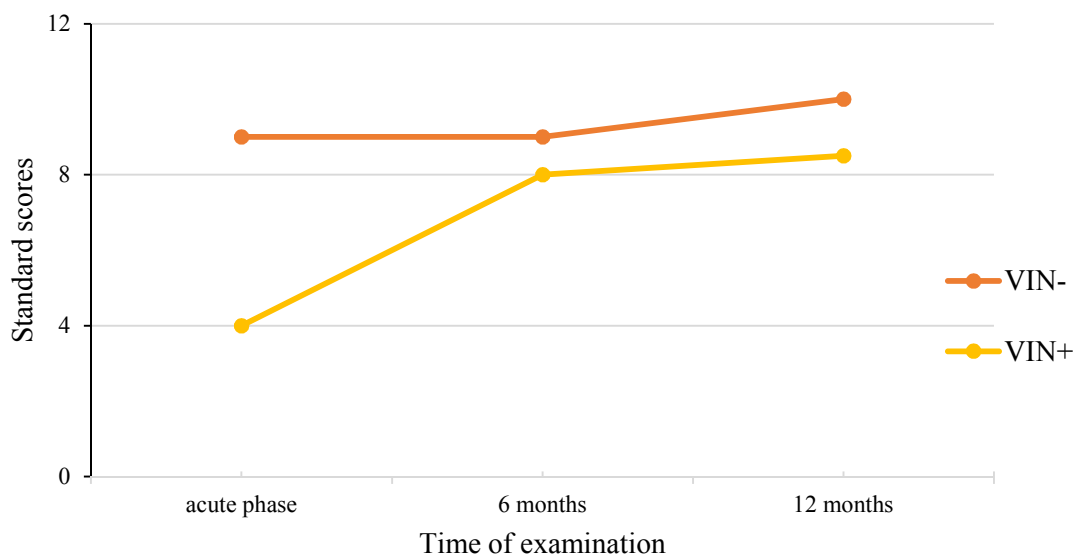


FIGURE 3. The VIN+ and VIN- groups' median standard scores in the Picture Completion task in the acute phase, at six months and 12 months.

3.3. Visual reasoning speed 12 months after stroke

The whole patient group spent more time finding the left-sided stimuli in the Picture Completion task ($Z = -3.525$; $p = <.001$). More detailed performance time analysis showed that VIN+ group spent significantly ($Z = -3.027$; $p = .002$) more time finding the left-sided items than the right-sided ones. Such a difference was not found in the VIN- group ($Z = -1.186$; $p = .236$). The median total performance times of both groups on left-sided and right-sided stimuli are presented in Figure 4.

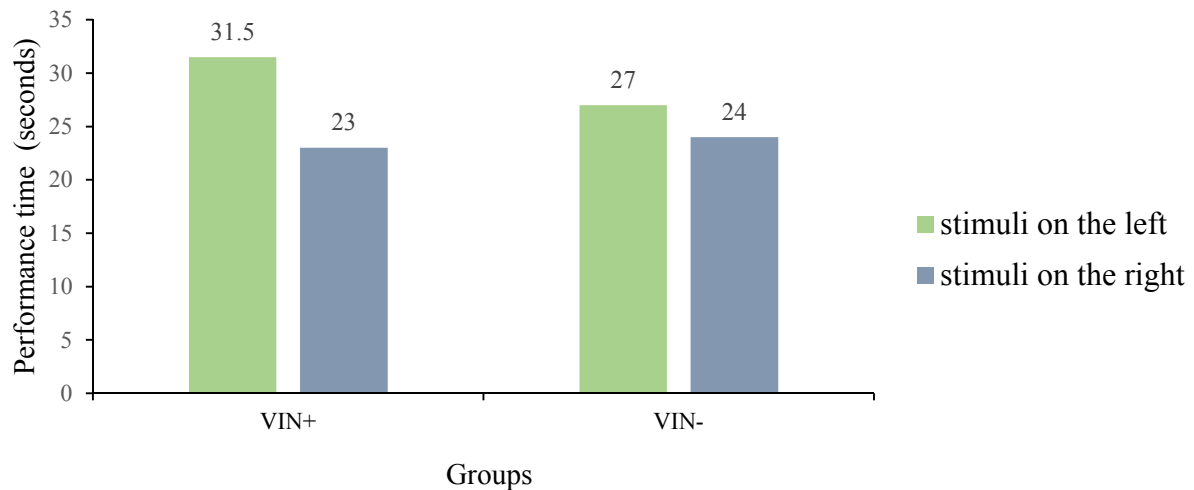


FIGURE 4. The median performance time of the first 12 items of the Picture Completion task with six left-sided (green) and with six right-sided (blue) stimuli in the visual inattention (VIN+) and non-inattention (VIN-) groups.

3.4. Group differences and changes in the starting points in the 12-month follow-up period

The SPs of the two patient groups and the HCs were analyzed. The median and the range of the SPs in the three cancellation tasks in all three examinations for all the groups are presented in the Table 5. In the acute phase the Kruskal-Wallis analysis of variance showed significant differences between the patient groups and the HCs in their SPs in all the cancellation tasks. At six months they differed in the line and star cancellation tasks, and at 12 months in the star cancellation SPs. A strong tendency towards significance ($p = .055$) was also seen in the letter cancellation task at 12 months.

More detailed multiple pairwise comparisons showed that in the acute phase the VIN+ group differed significantly from the VIN- group in the line and star cancellation tasks. In both tasks the SPs of the VIN+ group were more to the right. The VIN+ group differed also from the HCs in all the three tasks showing SPs located more to the right. The SPs of the VIN- group differed from the SPs of the HCs in the line cancellation task so that they (VIN-) were more to the left.

At six months the patient groups did not differ from each other but they both differed from the HCs in some of the tasks. The VIN+ group differed from the HCs in all the cancellation tasks (SPs of the VIN+ more to the right), and the VIN- group in the star cancellation tasks (the VIN- more on the right). In the 12-month examination there were no significant differences between the SPs of the patient groups. Differences between the VIN+ group and the HCs were found in the letter and star cancellation tasks in which the VIN+ group tended to start more from the right. At 12 months the SPs of the VIN- group were similar to those of the HCs'.

TABLE 5. Median and range of SP locations in the three cancellation tasks and comparisons between the VIN+, VIN- and HC groups.

Examination time and task	Group	<i>n</i> (missing)	Md (range)	Kruskal-Wallis	Compared pairs	Mann-Whitney U	<i>p</i>
I ACUTE PHASE							
Line cancellation	VIN+	16	+10.85 (-11.9–+12.3)	29.844; df=2; <i>p</i> =.001***	VIN+ vs. VIN-	-3.795	<.001***
	VIN-	9	-11.70 (-12.6– -11.3)		VIN+ vs. HC	-4.883	<.001***
	HC	50	-11.50 (-12.1–+11.6)		VIN- vs. HC	-2.374	.018*
Letter cancellation	VIN+	15 (1)	-11.60 (-11.6– +11.4)	13.644; df=2; <i>p</i> =.001***	VIN+ vs. VIN-	-1.372	.170
	VIN-	9	-11.60 (-11.6– -11.4)		VIN+ vs. HC	-3.690	<.001***
	HC	50	-11.60 (-11.6– -4.8)		VIN- vs. HC	-1.345	.179
Star cancellation	VIN+	16	+7.15 (-11.9–+14)	39.833; df=2; <i>p</i> <.001***	VIN+ vs. VIN-	-3.149	.002**
	VIN-	9	-11.90 (-11.9–+1.8)		VIN+ vs. HC	-6.225	<.001***
	HC	50	-11.90 (-11.9–+9.0)		VIN- vs. HC	-1.451	.147
II SIX MONTHS							
Line cancellation	VIN+	14 (2)	0.00 (-12.1–+12.4)	6.909; df=2; <i>p</i> =.032*	VIN+ vs. VIN-	-1.454	.146
	VIN-	9	-11.40 (-12.2–+4.0)		VIN+ vs. HC	-2.608	.009**
	HC	50	-11.50 (-12.1–+11.6)		VIN- vs. HC	-.561	.575
Letter cancellation	VIN+	13 (3)	-11.60 (-11.6– -8.4)	3.904; df=2; <i>p</i> =.142	VIN+ vs. VIN-	-.336	.737
	VIN-	9	-11.60 (-11.6– -11.4)		VIN+ vs. HC	-1.956	.050*
	HC	50	-11.60 (-11.6– -4.8)		VIN- vs. HC	-1.345	.179

TABLE 5. continues

Examination time and task	Group	<i>n</i> (missing)	Md (range)	Kruskal-Wallis	Compared pairs	Mann-Whitney U	<i>p</i>
Star cancellation	VIN+	16	-6.60 (-11.9–+13.5)	15.401; df=2; <i>p</i> =<.001***	VIN+ vs. VIN-	-.756	.449
	VIN-	9	-11.90 (-11.9–+2.3)		VIN+ vs. HC	-3.855	<.001***
	HC	50	-11.90 (-11.9–+9.0)		VIN- vs. HC	-2.188	.029*
III 12 MONTHS							
Line cancellation	VIN+	16	-12.00 (-12.0–+12.0)	3.347; df=2; <i>p</i> =.188	VIN+ vs. VIN-	-.198	.843
	VIN-	9	-12.00 (-12.0–+12.0)		VIN+ vs. HC	-1.399	.162
	HC	50	-11.50 (-12.1–+11.6)		VIN- vs. HC	-1.419	.156
Letter cancellation	VIN+	16	-11.60 (-11.6–+12.0)	5.784; df=2; <i>p</i> =.055	VIN+ vs. VIN-	-.444	.657
	VIN-	9	-11.60 (-11.6–+12.0)		VIN+ vs. HC	-2.442	.015*
	HC	50	-11.60 (-11.6– -4.8)		VIN- vs. HC	-1.412	.158
Star cancellation	VIN+	16	-11.90 (-11.9–+13.0)	8.081; df=2; <i>p</i> =.018**	VIN+ vs. VIN-	-.480	.631
	VIN-	9	-11.90 (-11.9–+9.0)		VIN+ vs. HC	-2.742	.006**
	HC	50	-11.90 (-11.9–+9.0)		VIN- vs. HC	-1.629	.103

VIN+ = visual inattention group; VIN- = non-inattention group; HC= healthy controls; *** = $p < .001$, ** = $p < .01$, * = $p < .05$

Table 6 presents the change in the BIT cancellation tasks' SPs during the first six months after stroke. The line cancellation SPs changed in both the VIN+ (shifting left) and VIN- groups (shifting right). In the letter cancellation task the SPs remained the same in both groups from the acute phase to six months. In the star cancellation task the SPs changed only in the VIN+ group (shifting left). There were no statistically significant changes in the SPs from six to 12 months in neither of the groups.

TABLE 6. The significance of SP change from the acute phase to six months in the VIN+ and VIN- groups and in the whole patient group.

Task	Z	VIN+ (n=16) <i>p</i>	Z	VIN- (n=9) <i>p</i>	Z	All (n=25) <i>p</i>
Line	2.271	.023*	-2.196	.028*	-.812	.417
Letter	-1.625	.104	0.00	1.00	-1.527	.127
Star	-2.342	.019*	-.524	.600	-1.691	.091

SP = starting point; VIN+ =visual inattention group; VIN- = non-inattention group; * = $p < .05$

4. DISCUSSION

The research questions of this thesis were set to study spontaneous recovery from left visual inattention in a 12-month follow-up in first-ever RH stroke patients ($n = 25$). The aim was to compare the visual reasoning abilities of the patients with and without left visual inattention three times: in the acute phase, and again at six months and 12 months after stroke. At 12 months, the laterality of the stimuli was taken into account and the performance time was also measured. In order to study the recovery from initial rightward bias the SPs in three cancellation tasks were analyzed in all examinations.

4.1. Main results

Suffering from visual inattention in the acute phase had a long-term negative impact on the patient's visual reasoning abilities and the visual reasoning speed. As expected, the VIN+ group showed more pathological SPs in the cancellation tasks which indicated the presence of initial rightward bias. Partial recovery from both lateralized and non-lateralized visual inattention was detected in the VIN+ group, especially during the first six months after stroke. Slower visual reasoning showed as a weaker performance in the Picture Completion task. In the acute phase, the VIN+ group's performance in the visual reasoning task was significantly weaker than that of the VIN- group, but during the following six months it improved so that there were no significant differences between the patient groups at six- or 12-month examinations. When the patient groups' scores were compared to the HCs', it became obvious that the VIN+ patients suffered from more severe decline in visual reasoning throughout the follow-up period. The percentage of patients performing within normal variation nonetheless grew in both of the groups throughout one year. Laterality of the visual stimuli affected the VIN+ group's performance even 12 months after stroke so that finding the left-sided stimuli took them significantly more time than finding the right-sided ones.

SP analysis in the BIT cancellation tasks showed that the VIN+ group had abnormal SPs in the line and star cancellation tasks in the acute phase, but their SPs shifted towards the left side of the sheet, especially during the first six months after stroke. At 12 months there were no significant differences in SPs between the VIN+ and VIN- groups. However, at that time the SPs of the VIN+ group differed significantly from those of the HCs and were still located more on the right. The median SPs of the VIN- group were located on the left side of the midline in all the examinations.

In their study, Nurmi et al. (2010) found that every third supposedly non-neglect RH patient suffered from visual inattention when SP analysis with task-specific guideline values was used. In this study the percentage was even higher: Of the 19 patients that did not suffer from visual neglect according to the conventional tests, 10 patients (52.6%) showed rightward bias indicating visual inattention. This is in line with the results by Jalas et al. (2002), who also found half the non-neglect patients showing rightward bias. Overall, 16 patients (64%) of this study group ($n = 25$) suffered from visual neglect or visual inattention in the acute phase after RH stroke.

4.2. Visual reasoning performances differed in the acute phase

The results of this study supported the hypothesis that visual inattention is often related to impaired and slow visual reasoning following RH stroke (Jehkonen et al., 2007; van Kessel et al., 2010) and that it may also come up when using tasks that are designed to measure other cognitive functions, especially if they include horizontally placed stimuli (Lezak, 2004).

The VIN+ and VIN- groups' performances in the Picture Completion task were compared in the acute phase, and significant differences in standard scores were found. Performing successfully in the Picture Completion task requires sufficient levels of visual recognition and adequate visual reasoning speed, since each item has a 20-second time limit (Wechsler, 1981). When the scores were compared to the healthy average (10), the median score of the VIN+ group was 4 indicating a moderate to severe impairment. The VIN- group on the other hand performed within normal variation: Their median standard score was 9.

Six months later the median score of the VIN+ group was 8 reaching the low average performance level. This indicates a significant recovery in visual reasoning and visual reasoning speed. The median score of the VIN- patients remained the same (9) and grew only by one point from six to 12 months. Therefore, it appears that their visual reasoning skills were not significantly impaired due to stroke. At six months, both of the groups performed within normal range although slightly under the average. Their scores did not change significantly from six to 12 months and differences between the groups were statistically non-significant both at the six- and 12-month examinations.

It is well established that RH patients with neglect are more likely to suffer from non-lateralized symptoms, such as slow visual processing, than other RH patients (Buxbaum et al., 2004). Also the initial rightward bias may slow down left-sided visual processing, since the patient tends to start his visual scanning from the right side (van Kessel et al., 2010). The results of this study replicated the previous finding that the most notable recovery from visual neglect occurs during the first two to six months after stroke (Appelros et al., 2004; Jehkonen, 2002b). Although the VIN+ group showed poorer performance in the acute phase, during the following six months they reached the performance level of the less impaired VIN- group.

4.3. Visual reasoning speed improved during the first six months after stroke

It was hypothesized that in the acute phase the VIN+ group's visual reasoning performance would be weaker than that of the VIN- group, but would improve during the follow-up period. The results supported the hypothesis: The performance of the VIN+ group improved by approximately four

standardized points during the first six months after stroke. This is in line with the previous finding that the most notable recovery from visual inattention happens during the first half a year after stroke (Appelros et al., 2004; Jehkonen, 2002b), and that the general non-lateralized symptoms decrease along the recovery from the lateralized ones (Husain & Rorden, 2003). The patient groups did not show significant improvement in visual reasoning from six to 12 months. The performance of the VIN- group remained the same during the one-year follow-up and most patients already performed within normal range in the acute phase. It can be assumed that their visual reasoning abilities were only mildly impaired due to stroke.

The patient groups differed only in the acute phase and the only significant change in performance occurred in the VIN+ group during the first six months after stroke. In order to get more detailed information about the level of performance of the patient groups, their scores were compared to the HC's. As expected, the VIN+ group showed more severe decline in visual reasoning abilities in all three examinations. During the one-year follow-up the severe decline percentage of the VIN+ group did, however, decrease from 37.5% to 18.8%, and at the same time the percentage of patients performing within normal range within the group grew from 31.3% to 62.5%. The trend was positive for the VIN- group, as well. Only 11.1% of the VIN- patients showed severe decline in the acute phase, and none during the later examinations. The percentage of the patients performing within normal variation grew during the year from 66.7% to 88.9%. The positive course of recovery was also seen between six and 12 months in both patient groups, although there were no statistically significant differences in the Picture Completion performance during that time.

4.4. The location of the stimuli affected visual reasoning speed

Initial rightward bias has been proven to be one of the most prominent symptoms of visual inattention (Jalas et al., 2002; Nurmi et al., 2010) and it is known to be long-standing (Kettunen et al., 2012). The results of this study supported these presumptions. It was hypothesized that even 12 months after stroke the rightward bias combined with slow visual processing would make it more challenging for the VIN+ group to find left-sided stimuli in the Picture Completion task. Results indeed showed a significant difference in the VIN+ group's performance times when the laterality of the stimulus was taken into account. The VIN+ patients took approximately 8.5 seconds longer to find the six left-sided stimuli compared to the six right-sided ones, whereas the difference in the VIN- patients was only three seconds being non-significant. Robertson et al. (1998) also found that even 8.5 months after RH stroke, patients with acute neglect became aware of left-sided visual stimuli more than half a second later than the right-sided ones. Slower processing of contralesional stimuli could be due to

a combination of the initial rightward bias that results in right-to-left scanning strategy, difficulties orienting to the left side of the body midline and a generally slow visual reasoning speed, which are all prominent symptoms of visual inattention (Jehkonen et al., 2007; Robertson & Halligan, 1999). Also the analysis on the background variables showed that the VIN+ group had more severe strokes which could contribute to the persistent slowness in visual reasoning. Previous studies have also suggested that stroke severity and the presence of persistent visual neglect are often related (Kettunen et al., 2012).

The results are in line with previous studies on the persistence of initial rightward bias (e.g. Kettunen et al., 2012). It is noteworthy, that also SP analysis at the end of the follow-up period showed that the VIN+ group still differed from the HCs in two out of three cancellation tasks exhibiting SPs more to the right. The VIN- group did not differ from the HCs in the 12-month examination.

4.5. Starting points differed between the groups and changed during the follow-up period

As hypothesized, the VIN+ group showed more abnormal SPs in the acute phase. It is well established that initial rightward bias, which is common among patients with visual inattention (Jalas et al., 2002), often becomes apparent in BIT cancellation tasks' SP analysis (Azouvi et al., 2002; Nurmi et al., 2010). In the acute phase the VIN+ group showed a strong tendency to start the line and star cancellation tasks from the right side: The median SP in the line cancellation task was located on the far right, 10.85 cm from the centre, and the star cancellation SP was 7.15 cm to the right of the centre of the sheet. VIN- group on the other hand had median SPs far on the left. Differences between the patient groups in these two SPs were significant. The results are in line with the conclusions stated by Nurmi et al. (2010), who suggested that the line and star cancellation tasks are more sensitive in detecting visual inattention than the letter cancellation task, and should therefore be used whenever assessing the presence of visual neglect.

Interestingly enough, the median letter cancellation SPs of the VIN+ group on the other hand were located on the far left in all examinations and did not differ from the SPs of the VIN- group. They did however differ from the SPs of the HCs throughout the follow-up period locating more on the right. Jalas et al. (2002) studied the rightward bias of visual neglect patients and found that the fewest right starts in the cancellation tasks were seen in the letter cancellation task, although the percentage was still 62.5%. On the other hand, the same study showed that the non-neglect RH stroke patients displayed a strong tendency to start the search from the right in the same task when compared to HCs, which would suggest that the task is sensitive in detecting rightward bias.

When compared to the HCs, the VIN+ group exhibited more abnormal SPs throughout the follow-up period and the groups differed in all but the line cancellation task at 12 months. In all the tasks the VIN+ group started more on the right. Also previous studies have shown that initial rightward bias is a prominent and long-standing symptom following the impairments in the attentional functions after stroke (Kettunen et al., 2012).

The SPs of the VIN- group were quite similar to those of the HCs' and they differed from each other only in two tasks. Pairwise comparisons showed that the VIN- group differed from the HC group in the line cancellation task in the acute phase, and in the star cancellation task at six months. In the line cancellation task the VIN- group started more from the left. Further analysis showed, that all the VIN- patients ($n = 9$) had started their task on the left side of the task-specific guideline value (-5.85 cm) set by Nurmi et al. (2010), while 88% of the HCs had done the same. The differences found between the groups may be due to wider range of SPs in the HCs. The group median SPs were both located on the far left. From previous studies it is known that although HCs usually show a strong tendency to start from the far left, 5–29% of them use the opposite strategy and start their visual scanning from the right (Azouvi et al, 2006; Kettunen et al., 2012; Nurmi et al., 2010).

In the star cancellation task the SPs of the VIN- group were more to the right: 55.6% of the patients started their task from the left side of the guideline value (-11.05 cm) while 86% of the HCs had normal starts. It is noteworthy, that the VIN- group was fairly small ($n = 9$) and therefore even two or three abnormal SPs affect the group level performance. Also in this task the group medians were similar to each other. At 12 months no significant differences were found between these groups. The results are comparable to those of Nurmi et al. (2010), who found that in the acute phase the non-neglect group differed from the HCs in the star cancellation task and a tendency towards significance was seen in the line cancellation task, as well.

Significant changes in the patients' SPs were detected during the first six months after stroke. Both the line and star cancellation SPs of the VIN+ group shifted left, indicating a decrease in initial rightward bias. Also previous studies have shown that the BIT cancellation tasks' SPs tend to change and shift left, along the recovery from visual inattention (Jalas et al., 2002; Kettunen et al., 2012). Kettunen et al. (2012) studied 43 RH stroke patients and 49 HCs during a six-month follow-up, and found that although the rightward bias exhibited by the visual neglect group decreased, the only significant change in the SP was seen in the line cancellation task.

Also the SPs of the VIN- group in the line cancellation task changed from the acute phase to six months, but surprisingly they shifted towards the right. It seems that at six months the range of the VIN- group's line cancellation SPs was wider (from -12.2 to +4.0 cm) than in the acute phase (from -12.6 to -11.3 cm). Further analysis showed that at six months two VIN- patients had SPs to right

from the guideline value (-5.85 cm). Also here the small size of the group could affect the results. Right starts are also seen in HCs (e.g. Nurmi et al., 2010). Change for the worse in the SPs could also be a sign of cognitive deterioration, which is fairly common after stroke (Hochstenbach et al., 2003).

There were no significant changes in the SPs of neither of the patient groups from six to 12 months. Therefore, it seems that the most notable spontaneous recovery from visual inattention occurred during the first six months after stroke – a finding that has come up in previous studies, as well (Jehkonen, 2002b; Jehkonen et al., 2007).

4.6. Limitations and strengths of the study

There is a current need for study on visual inattention: it has not been studied as much as visual neglect since the conventional methods have not always been sensitive enough to detect it. The condition can nonetheless risk the safety and independent functioning of the patient in everyday life. Detecting visual inattention in time would improve the quality of rehabilitation and prevent further problems, e.g. at work. Using the SP analysis especially with the line and star cancellation tasks as part of the conventional neuropsychological examination could bring more accuracy in the evaluation of attentional impairments.

Deficits in visual reasoning are frequently present in patients with visual inattention and visual neglect. These impairments may show in various everyday situations, especially in complex or challenging environments. Using the Picture Completion task in this study provided information about both the general level of visual reasoning (sum scores) and the particular quality of visual reasoning speed performance with laterally placed stimuli on the ipsilesional or contralesional peripersonal space in a limited time-setting. The Picture Completion task measures visual reasoning, but in this study it was applied in two new ways: The laterality of the stimuli was taken into account and the exact time spent on each stimulus was measured 12 months after stroke. This has not been previously studied. It is noteworthy that 12 months after stroke there was still a significant difference between the patient groups in visual processing speed of differently lateralized stimuli.

The patient sample was rather small and focused only on first-ever RH stroke patients, which may lower the generalizability of the results. There were only nine patients that did not show visual inattention in the acute phase. The results were, however, mostly in line with many previous studies, which increases the reliability of the study.

The study provided new and detailed information about the visual reasoning abilities of the VIN+ patients in three examinations. A longitudinal research setting gave more reliable information of the

course of the patients' spontaneous recovery. One of the strengths of this study was that the presence of visual neglect and visual inattention was assessed using both conventional cancellation tasks and SP analysis. Furthermore, these were combined with the visual reasoning task, where laterality of the stimuli and performance time were also taken into account. The results clearly showed that the SP analysis with the guideline values set by Nurmi et al. (2010) was a sensitive tool to distinguish the visual inattention patients from the patients without visual inattention as well as from HCs. Using several methods when assessing visual inattention can provide valuable additional information about the condition.

The results replicated the previous finding that spontaneous recovery from visual inattention occurs especially during the first six months after RH stroke. The recovery was seen on both lateralized and non-lateralized functions, such as initial rightward bias and slow visual reasoning. Interestingly, when the visual reasoning scores were compared to standardized norms the improvement in performance levels seemed to continue on a subtle level after six months. Further research with an even longer follow-up period could shed more light on this issue. It would also be interesting to compare patients receiving rehabilitation to those who do not receive it.

When the population ages, stroke becomes more frequent. It puts a tremendous burden on the health care system and causes an immeasurable amount of human suffering. Preventing stroke is essential, but after stroke it is important to focus on an effective neuropsychological examination and rehabilitation. Detecting cognitive disorders and their special characteristics following stroke in optimal time will improve the prognosis by helping the patients recover sooner with an adequate rehabilitation plan.

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