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VISUOATTENTIVE DEFICITS IN UNILATERAL STROKE—ASSESSMENT OF VARIOUS ASPECTS WITH COMPUTER-BASED METHODS

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DOCTORAL DISSERTATION

To be presented for public discussion with the permission of the Faculty of Medicine of the University of Helsinki, in Biomedicum Helsinki 1, Lecture Hall 2, on the 21st of June, 2022 at 12 o'clock.

Helsinki 2022

Doctoral Programme in Clinical Research (KLTO)

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ISBN 978-951-51-8195-4 (pbk.)
ISBN 978-951-51-8196-1 (PDF)

Unigrafia
Helsinki 2022

ABSTRACT

Stroke is known to be among the most common causes of long-term disability worldwide, and cognitive symptoms especially affect patients' recovery and return to everyday life. Attention deficits are among the most typical cognitive symptoms after stroke, even with patients who experience good clinical recovery. Hemispatial neglect is a dramatic example of stroke disturbing attention as the patient's attention is oriented toward the side of the brain lesion (i.e., the ipsilesional side) while the patient ignores the side opposite the brain lesion (i.e., the contralesional side). Severe neglect has been associated with poor functional outcomes, but even milder deficits can cause significant real-life problems. Traditionally, neglect has been diagnosed with paper-and-pencil methods assessing visual attention. These tests are still widely used. Severe neglect becomes easily evident with conventional methods, but milder deficits are more demanding to diagnose. Growing evidence indicates that traditional tests are not sensitive in detecting mild forms of neglect.

The present set of studies aimed to examine whether visuoattentive deficits of stroke patients could sensitively be uncovered with computer-based methods. A novel large-screen computer method was developed, and another computer test battery was used. First, two large-screen dual tasks were compared, and their complexity was varied, in order to reveal even subtle visual neglect (Study I). Then, two computer methods with different qualities were used to find out whether unilateral stroke patients show both contralesional and general (nonlateralized) deficits in visual attention (Study II). Last, a traditional cancellation task was converted into a digital large-screen format. This large-screen cancellation task was then compared with standard-screen dual tasks to find out which one would be more sensitive in revealing signs of visual neglect (Study III): the large-screen format or the dual-task approach.

Forty patients, each diagnosed with first-ever neuroradiologically verified stroke either in the left hemisphere (LHS patient group, n = 20) or the right hemisphere (RHS patient group, n = 20), and 20 healthy controls participated in the study. Patients were examined on average 106 days poststroke. All participants underwent a comprehensive neuropsychological examination containing conventional tests, and assessments with seven computer-based methods. Four large-screen tasks were developed, and three other computer tasks were used. The large-screen test battery contained two visual dual tasks, a novel cancellation task, and a task with visual stimuli in fast downward motion. The standard-screen battery contained a visual single task in which brief unilateral and bilateral targets were presented, as well as two dual tasks analogous with the single task but with a visual or auditory secondary task.

RHS patients showed subtle visual neglect and/or extinction in large-screen and standard-screen dual tasks, and visual extinction in a standard-screen single task. Both patient groups showed general visual inattention for stimuli presented in fast downward motion. However, neither paper-and-pencil nor the large-screen cancellation tasks were able to identify these deficits. The performance of LHS and RHS patients was significantly deteriorated in relation to the controls in several neuropsychological tests assessing executive functions and processing speed, but neither patient group differed from the other.

In conclusion, computerized methods can offer sensitive and ecologically valid clinical assessment tools of visuoattentive deficits, which are subtle and remain undetected through traditional neuropsychological tests. Even these subtle deficits are important to diagnose because they could cause significant real-life problems.

TIIVISTELMÄ

Aivoverenkiertohäiriöt aiheuttavat yhden merkittävimmistä inhimillisistä ja taloudellisista tautitaakoista maailmanlaajuisesti. Erityisesti kognitiivisten oireiden on todettu heikentävän potilaiden toipumista, sekä aiemman kaltaiseen arkeen ja työhön palaamista. Tarkkaavuuden häiriöt ovat yleisimpiä aivoverenkiertohäiriön jälkeisiä kognitiivisia oireita, myös potilailla, joiden neurologinen toipuminen on muutoin erinomaista. Toispuoleinen huomiotta jääminen eli nk. *neglect* on yleinen tarkkaavuuden häiriö aivoverenkiertohäiriön jälkeen. Neglectin seurauksena aivovaurion vastakkaisen puolen ympäristön ja osalla potilaista myös kehon puolen huomioiminen on puutteellista. Vaikea-asteinen neglect heikentää itsenäistä arkiselviytymistä, mutta myös lieväasteinen häiriö saattaa aiheuttaa merkittäviä arkipäivän ongelmia. Neglectin diagnosointiin on perinteisesti käytetty näönvaraisen tarkkaavuuden arviointiin kehitettyjä kynä-paperi-menetelmiä. Nämä menetelmät ovat yhä laajalti kliinisessä käytössä ja ovat tarkoituksenmukaisia vaikea-asteisen neglectin toteamisessa. Lieväasteisen häiriön diagnosointi on kuitenkin haastavaa ja tutkimusnäytön perusteella perinteiset menetelmät ovat tähän tarkoitukseen riittämättömiä.

Tämän tutkimussarjan tarkoituksena oli tarkastella tietokonepohjaisten arviointimenetelmien kykyä havaita aivoverenkiertohäiriön jälkeisiä näönvaraisen tarkkaavuuden häiriöitä. Tutkimusta varten kehitettiin uusi tietokonepohjainen menetelmä, jossa hyödynnettiin laajaa näköhavaintokenttää, sekä käytettiin toista tietokonepohjaista näönvaraisen tarkkaavuuden arviointipatteristoa. Ensimmäisessä osatutkimuksessa verrattiin kahta vaikeustasoltaan erilaista testiä, joissa molemmissa suoritettiin kahta näönvaraista tehtävää rinnakkain (nk. kaksoistehtävä) ja jotka esitettiin laajassa havaintokentässä. Tarkoituksena oli tarkastella menetelmien herkkyyttä havaita lieväasteinen neglect. Toisessa osatutkimuksessa verrattiin kahta ominaisuuksiltaan erilaista testiä, joiden oletettiin tuovan esiin näönvaraisen tarkkaavuuden häiriöiden eri ulottuvuuksia. Toisessa testeistä esitettiin nopeassa alaspäin suuntautuvassa liikkeessä olevia ärsykkeitä laajassa näköhavaintokentässä ja toisessa lyhytkestoisesti standardikokoisen näytön laidoilla välähtäviä ärsykkeitä (oikealla, vasemmalla tai yhtä aikaa molemmilla laidoilla). Tarkoituksena oli selvittää kärsivätkö potilaat toispuoleisen huomiotta jäämisen lisäksi myös yleisestä eli ei pelkästään aivovaurion vastakkaisen puolen toimintatilaan rajoittuvasta näönvaraisen tarkkaavuuden häiriöstä. Kolmannessa osatutkimuksessa kehitettiin uusi näönvaraisen etsinnän testi, jossa hyödynnettiin perinteistä (nk. *cancellation task*) testauslähestymistapaa, mutta joka muunnettiin tietokonepohjaiseksi ja esitettiin laajassa havaintokentässä. Uuden testin herkkyyttä havaita neglect verrattiin kahteen standardikokoisella näytöllä esitettävään kaksoistehtävään, joissa koehenkilöiden täytyi havaita näytön laidoilla (oikealla, vasemmalla tai yhtä aikaa molemmilla laidoilla) välähtäviä näköärsykkeitä ja suorittaa samanaikaisesti joko näkö- tai kuuloärsykkeiden prosessointiin perustuvaa rinnakkaistehtävää.

Tutkimukseen rekrytoitiin 40 ensimmäiseen diagnosoituun aivoverenkiertohäiriöönsä sairastunutta kuntoutuspotilasta, sekä 20 tervettä kontrollikoehenkilöä. Potilaiden verenkiertohäiriö sijoittui joko oikeaan (20 potilasta) tai vasempaan (20 potilasta) aivopuoliskoon ja heidän tutkimuksensa toteutettiin keskimäärin 106 päivää sairastumisen jälkeen. Tutkimus piti sisällään neuropsykologisen arvion, jossa koehenkilöiden kognitiivisia toimintoja arvioitiin perinteisillä kynä-paperi-menetelmillä, sekä seitsemän tietokonepohjaista testiä, joista neljässä hyödynnettiin laajaa näköhavaintokenttää ja kolmessa standardikokoista tietokonenäyttöä.

Oikean aivopuoliskon verenkiertohäiriöpotilailla kaksoistehtävät, sekä laajassa näköhavaintokentässä että standardikokoisella näytöllä esitettynä, toivat esiin lievään neglectiin viittaavia löydöksiä. Oikean aivopuoliskon verenkiertohäiriöpotilailla tuli esiin

vasemmanpuoleiseen huomiotta jäämiseen viittaavia löydöksiä myös ärsykkeillä, jotka esitettiin yhtä aikaa standardikokoisen näytön oikealla ja vasemmalla laidalla (nk. *extinction*-ilmiö; vasemman puolen ärsykkeet jäävät huomiotta, kun ne esitetään yhtä aikaa oikean puolen ärsykkeiden kanssa). Lisäksi sekä oikean että vasemman aivopuoliskon verenkiertohäiriöpotilailla oli nähtävissä yleistä tarkkaamattomuutta testissä, jossa esitettiin nopeassa alaspäin suuntautuvassa liikkeessä olevia näköärsykkeitä laajassa havaintokentässä. Näitä ilmiöitä ei ollut nähtävissä perinteisillä nk. cancellation-testeillä tietokonepohjaisesti tai kynä-paperi-versiona esitettynä. Molemmat potilasryhmät suoriutuivat kontrollikoehenkilöitä merkitsevästi heikommin neuropsykologisen tutkimuksen toiminnanohjausta ja prosessointinopeutta arvioivissa osioissa, mutta potilasryhmien suoritukset eivät poikenneet toisistaan.

Yhteenvetona tämän väitöskirjan tutkimuksista voidaan todeta, että tietokonepohjaisilla menetelmillä voidaan saada esiin lieviä aivoverenkiertohäiriön jälkeisiä näönvaraisen tarkkaavuuden häiriöitä, jotka eivät tule perinteisillä menetelmillä esiin. Myös lievien häiriöiden diagnosointi on tärkeää, koska ne voivat aiheuttaa merkittäviä arkiselviytymisen ongelmia.

ACKNOWLEDGEMENTS

This project has been completed as part of a multiprofessional cooperation between the Helsinki University Hospital (HUH) Neurocenter, Division of Neuropsychology, and the Aalto University, Department of Electrical Engineering and Automation. We have also cooperated closely with renowned researcher, Dr. Mario Bonato, from the Department of General Psychology of the University of Padova. The multicultural and multiprofessional group of researchers has introduced me to the fascinating world of science in a supportive, helpful, and educational environment. Above all, working with these esteemed colleagues has been fun, as all our work has been enveloped in an atmosphere of positivity—and humor! This research project, and dissertation, took several years to complete. During this time, I have worked as both a researcher and in a clinical setting, completed my specialization in neuropsychology, and became a mother. Combining all of this would never have been possible without a broad group of incredible people with whom I have been fortunate enough to cross paths, and who shall always have my utmost gratitude.

First, I wish to express my deepest gratitude to my supervisor and closest mentor, Docent Marja Hietanen, who has incessantly encouraged and supported me in both my research and clinical neuropsychology since the early days of my career. She has generously shared her amazing expertise and contacts with me, and has spent innumerable hours of her personal time to advance this project as well as my dissertation. I have always been able to rely on her completely and without reservation—in both the good times as well as the challenging ones. My indebtedness to her is indescribable. I'm also deeply grateful to my supervising professor, Professor Kimmo Alho at the Department of Psychology and Logopedics, for his encouraging support, competent guidance, and insightful comments for the manuscripts, which I always received promptly.

I'm forever grateful to Professor Raimo Sepponen and Mr. Matti Linnavuo, L. Tech, whose innovation and initiative were the primary force behind this project. Raimo has been central in method development and conceptualizing, and has been invaluable in the process of applying for research grants. Matti has likewise been crucial in method development and conceptualizing, and has been responsible for the technical setup of the new methods. He has been untiring in his willingness to offer technical support, and has taken a significant role in ensuring the accurate description of our methods in the manuscripts. I owe my profound gratitude to Docent Hanna Jokinen for her never-ending helpfulness and encouragement, and for sharing her extensive expertise with me. It was Hanna's proactivity and contacts that enabled us to collaborate with Dr. Mario Bonato. I'm deeply grateful to Dr. Mario Bonato for his extensive support, guidance, and encouragement. Sharing his method and amazing expertise in the field of visuospatial attention was indispensable for me to be able to finish this dissertation. Ms. Outi Vuori, M. Psych, deserves my heartfelt thanks for advancing the research project, which had been crucial especially during my maternity leave.

I wish to express my sincerest gratitude to Mr. Tage Orenius, L. Psych, and Professor Heikki Hurri, together with the personnel of Orton, and to Orton's research funding, for their significant contribution and support at the early phases of the project.

I owe special thanks to Mr. Jari Lipsanen, M. Psych; Ms. Paula Bergman, M. Sc.; and Dr. Alessio Toraldo for their competent guidance in the field of statistics, to Docent Viljami Salmela for sharing his expertise on visual perception, and to Valtteri Kaartemo, April White, and Alyson Linefsky for proofreading the manuscripts.

My heartfelt thanks go to our team “Doctors in spe”: Kristiina Relander, Kaisa Mäki, and Sanna Liesto—thank you for your friendship, support, and insightful comments when preparing the manuscripts. Kristiina, thank you for sharing the ups and downs during all these years, and being so encouraging and helpful. I’m very grateful for our friendship. I also feel deeply grateful to the rest of my colleagues at HUH Neuropsychology for being flexible in their own work to help our project to advance, for assisting in patient recruitment, and for sharing their scientific expertise.

My warm and humble thanks go to all of the participants who generously gave their time in taking part in this research and thus made it possible.

I wish to express my sincerest gratitude to the official reviewers Docent Mira Karrasch and Docent Erja Poutiainen for their competent and insightful comments. It is a privilege for me to have Docent Mervi Jehkonen as the opponent. Her expertise in my research field is internationally recognized.

Concluding this project and my dissertation would not have been possible without external financing, for which I am extremely grateful to the Oskar Öfflunds Stiftelse sr. and Alfred Kordelin foundation, the HUS Neurocenter, and the Employment Fund, which enabled my postgraduate studies.

Finally, warm and loving thanks to all my friends, and the whole family for their amazing support and love. Reaching the end of this project was only possible because of the incessant love and nurturing that our children received from their grandparents during all these years. To my parents, Liisa and Esko, thank you for always being there, in every possible way. Ultimately, I am ever grateful and most indebted to Daniel for his immense help and support in so many ways. Oscar and Victor, my precious ones, thank you for introducing me to the greatest miracle of life.

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

The present dissertation is based on the following original articles, referred to in the text by Roman numerals (Studies I–III).

I. Villarreal, S., Linnavuo, M., Sepponen, R., Vuori, O., Jokinen, H. & Hietanen, M. (2020). Dual-task in large perceptual space reveals subclinical hemispatial neglect. *Journal of the International Neuropsychological Society, 26*, 993–1005.

II. Villarreal, S., Linnavuo, M., Sepponen, R., Vuori, O., Bonato, M., Jokinen, H. & Hietanen, M. (2021). Unilateral stroke: computer-based assessment uncovers non-lateralized and contralesional visuoattentive deficits. *Journal of the International Neuropsychological Society, 27*, 959–969.

III. Villarreal, S., Linnavuo, M., Sepponen, R., Vuori, O., Bonato, M., Jokinen, H. & Hietanen, M. (2022). Computer-based assessment: dual-task outperforms large-screen cancellation task in detecting contralesional omissions. *Frontiers in Psychology,* 12, 6284.

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ABBREVIATIONS

AI	Asymmetry index
ANOVA	analysis of variance
B-W	Bourdon–Wiersma
BIT	Behavioral Inattention Test
CT	computed tomography
df	degree of freedom
FIM	Functional Independence Measure
HUH	Helsinki University Hospital
ISI	interstimulus interval
ITI	intertarget interval
LHS	left hemisphere stroke
LTCT	Lateralized Targets Computer Task
MPH	Mean Position of Hits
MRI	magnetic resonance imaging
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
PnP	paper-and-pencil
RGB	red, green, and blue color-model triplet
RHS	right hemisphere stroke
RT	reaction time
SD	standard deviation
SP	starting point
SPSS	Statistical Package for Social Sciences
TM	Trail-Making Test
TM A	Trail-Making Test, Part A
WMS-III	Wechsler Memory Scale, third edition

1 INTRODUCTION

1.1 STROKE

1.1.1 INCIDENCE AND DEFINITION

The global human, social, and economic burden caused by strokes is extensive (Feigin et al., 2014; Wolf, 2004). Worldwide, stroke is the second highest cause of death, and the leading cause for long-term neurological disability in adults (Lozano et al., 2012; Strong et al., 2007). In 2010, almost 17 million people suffered stroke, nearly six million died, and there were about 102 million functional life years lost (Feigin et al., 2014). The incidence of stroke in Finland has been estimated at 82,000, which is the equivalent of 1.5% of the population (Meretoja et al., 2010b). Finnish estimates place the overall lifelong healthcare costs of each single patient from stroke onward at 80,000 euros, and the overall annual national costs at 1.1 billion euros (Meretoja et al., 2010a).

Stroke is an episode of acute neurological dysfunction caused by impairment of cerebral circulation (Sacco et al., 2013). Strokes can be grouped into two major categories: ischemic and hemorrhagic. Ischemic stroke is caused by an occlusion of the artery supplying oxygen and glucose to brain cells, resulting in focal infarction (Sacco et al., 2013). Hemorrhagic strokes are caused by a rupture of a blood vessel. Two main types are intracerebral hemorrhage, defined as focal collection of blood within the brain tissue or cerebral ventricles, and subarachnoid hemorrhage, defined as bleeding into the subarachnoid space (Sacco et al., 2013). About 87% of strokes are ischemic, 10% are intracerebral hemorrhage, and 3% are subarachnoid hemorrhage (Rosamond et al., 2008).

1.1.2 MAJOR RISK FACTORS

There are several risk factors for stroke. In their case-control study (n = 6000), O’Donnel and colleagues (2010) listed the ten most significant risks. These were hypertension, smoking, excessive alcohol consumption, unhealthy cardiovascular diet, low physical activity, high waist-to-hip ratio, diabetes mellitus, psychosocial stress/depression, cardiac causes, and high ratio of apolipoproteins B to A1. Together these accounted for almost 90% of the population-attributable risk for stroke.

Although some of the risk factors cannot be addressed, such as age (Hyvärinen et al., 2010; Seshadri et al., 2006), gender (Hyvärinen et al., 2010), and genetic predisposition factors (Bevan et al., 2012; Traylor et al., 2012), many of them are treatable. These include lifestyle factors and treatable illnesses. Increased blood pressure is among the most significant treatable risk factors, as it explains about 60% of the global stroke burden (Lawes et al., 2004). Blood pressure levels above 115/75 mm Hg raise the risk continuously (Lawes et al., 2004). On the other hand, a 10 mm Hg reduction toward the risk limit decreases the probability of stroke by about one third (Lawes et al., 2004; Lewington et al., 2002).

1.1.3 TREATMENT, MULTIDISCIPLINARY REHABILITATION, AND OUTCOME

The incidence of and mortality rates due to stroke have declined in high-income countries, due mostly to progress in prevention and treatment (Feigin et al., 2009; Harmsen et al., 1992; Li et al., 2020; MacKay & Mensah, 2004; Sarti et al., 2000). In addition to preventive measures relating to lifestyle and treatable illnesses, positive development is also due to optimized acute-stroke care. Rapid access to treatment materially affects the prognosis (Strbian et al., 2010). In a case of ischemic strokes, endovascular recanalization therapy, enabled by early diagnostics, significantly improves the outcome (Emberson et al., 2014; Goyal et al., 2016; Hacke et al., 2004). Commencement of rehabilitation without delay is also key for good recovery. Patients receiving treatment and multidisciplinary rehabilitation in a specialized stroke unit show lower mortality, shorter-term inpatient care, and higher probability to be discharged, as compared to those receiving other kinds of inpatient care (Jorgensen et al., 2000; Pereira et al., 2012; Stroke Unit Trialists' Collaboration, 2007). Stroke patients of all ages benefit from organized multidisciplinary rehabilitation in the early phase of recovery irrespective of the severity of stroke (Jorgensen et al., 2000; Langhorne & Duncan, 2001; Rønning & Guldvog, 1998). These advantages are long-term (Indredavik et al., 1999; Pereira et al., 2012).

1.1.4 COGNITIVE SYMPTOMS

Despite the progression in treatment, stroke can lead to devastating outcomes among survivors (Elkind, 2009), and cognitive deficits especially affect patients' recovery and return to everyday life (Barker-Collo & Feigin, 2006; Duncan et al., 2000). In a population-based study of Patel and colleagues (2002; n = 645), 38% of the patients showed clear impairments in a cognitive screening test. These deficits became evident at 3 months poststroke but were also associated with poor long-term outcome (see also Oksala et al., 2009). Other studies, using more comprehensive test batteries, have reported even greater incidences (Jokinen et al., 2015; Kauranen et al., 2013; Kauranen et al., 2014), also among patients who otherwise had recovered well. In a cohort study of Jokinen et al. (2015; n = 409, mean age 71), the prevalence of cognitive symptoms in at least one domain was 83% at 3 months poststroke. Even among those who showed excellent clinical recovery, cognitive impairment of some degree has been identified in as many as 71% of stroke patients (Jokinen et al., 2015). Another cohort study (Kauranen et al., 2014), assessing slightly younger patients with first-ever stroke (n = 223, mean age 54), found at least one cognitive deficit in 61% of cases at 8 days poststroke and in 46% at 6 months poststroke. Similar figures have also been reported earlier (see, e.g., review by Gottesman & Hillis, 2010). The cognitive domains typically affected are executive functions; attention; information processing; psychomotor speed; memory; visuoperceptual, constructional, and spatial skills; language; and arithmetic processing (Hochstenbach et al., 2001; Hurford et al., 2013; Jokinen et al., 2015; Kauranen et al., 2014; Nys et al., 2005). There is some variation as a function of lesion site; for example, deficits in language, verbal memory, and abstract reasoning are typical specifically after stroke affecting the left hemisphere, whereas stroke affecting the right hemisphere commonly results in deficits in visual perception and construction, as well as visuoattentive and spatial functions (Barker-Collo & Feigin, 2006; Nys et al., 2007). Attention deficits are among the most typical symptoms experienced by patients with good clinical recovery, and they also predict long-term outcome (Jokinen et al., 2015; Robertson et al., 1997b; Stephens et al., 2004).

1.2 ATTENTION

Attention is a prerequisite for most cognitive functions. It refers to an orientation of information processing with respect to motivation and task (Jehkonen et al., 2015). It has two major aspects: selectivity, which refers to directing attention to prominent or important items, and intensity, which determines the ability to inhibit irrelevant information outside the focus of attention (Spikman & van Zomeren, 2010). In this sense, attention reflects the quality of information processing as it tunes the focus and level of intensity properly with respect to the task at hand (Spikman & van Zomeren, 2010). Attention consists of several subprocesses rather than a single factor. A unified neuropsychological model of attention (Cohen, 2014) proposes four distinct, but interrelated, attentional elements. *Sensory selection* refers to an early-phase information processing, during which sensory information is filtered, and attention is focused and automatically shifted. Selectivity is crucial in attention, as the capacity of information processing is limited. *Executive attention* is related to information processing with a premeditated goal. Responses are selected, initiated, inhibited, and switched, based on intention. The whole process is supervised by an executive control. A third element is *focused attention and capacity*. Several factors affect attentional resources, and they include, for example, capacity of sensory and working memory, executive functions, and processing speed, as well as motivation and effort (Cohen, 2014; Jehkonen et al., 2015). In healthy persons, the most significant factor affecting attention is alertness, which varies, for example, as a function of circadian rhythm, quality and amount of sleep, medication, and psychological distress (Jehkonen et al., 2015). Attention, executive functions, and working memory are strongly interrelated, and their cooperation is emphasized, for example, in situations requiring the management of two or more tasks simultaneously (cf., divided attention, dual tasking, multitasking) (Jehkonen et al., 2015). The last attentional element is *sustained attention*. The significance of the ability to maintain a vigilant state, or sustained attention, is emphasized in long-lasting tasks. Hence, *sustained attention* can be seen as temporal distribution and the "end product" of other elements (Cohen, 2014).

1.2.1 NEURAL NETWORKS OF ATTENTION

Posner and Petersen (1990; see also Petersen & Posner, 2012) proposed that the attention system can be divided into three networks: 1) *an alerting network*, which maintains a vigilant state (i.e., sustained attention); 2) *an orienting network*, which is essential in orienting to external events in space (e.g., selective and focused attention for visual stimuli); and 3) *an executive network*, which plays an important role in top-down control of attention.

The orienting and *executive networks* can further be divided into two subsystems. *The orienting network* contains the dorsal and the ventral networks (see also Corbetta & Schulman, 2002, 2011). The dorsal network has been associated with goal-directed (top-down) stimulus selection and responses, and the ventral network with (bottom-up) orienting to salient stimuli outside the focus of attention. Subsystems of *the executive network* contain the frontoparietal control system, recruited for task initiation, switching, and adjustments; and the cingulo-opercular system, associated with a stable background maintenance for task performance as a whole.

According to brain imaging findings (see, e.g., Corbetta & Schulman, 2002, 2011; Petersen & Posner, 2012; Vossel et al., 2014), *the alerting network* includes brainstem arousal systems, as well as regions in the frontal and parietal areas. The dorsal component of *the orienting network* appears to form a bilateral system, and covers the frontal eye fields as well as the intraparietal sulcus of each hemisphere. Regions of the dorsal system contain retinotopically organized maps of contralesional space (Vossel et al., 2014). These areas might therefore be specifically important in spatial attention, as they may represent behavioral salience of locations in the visual field (Chelazzi et al., 2014; Vossel et al., 2014). The ventral component of *the orienting network* appears to be lateralized to the right hemisphere, and consists of the temporoparietal junction and the ventral frontal cortex. Current theories of visual attention suggest that orienting to visual stimuli is modulated—not just by bottom-up but also by top-down signals of both the ventral and dorsal systems: top-down signals, reflecting expectations, might have influence on the visual salience of objects and, hence, on the function of the bottom-up system (Corbetta & Schulman, 2002). Figure 1 presents a simplified demonstration of the dorsal and ventral visual attention systems in the brain (modified from the illustration by Vossel et al., 2014).

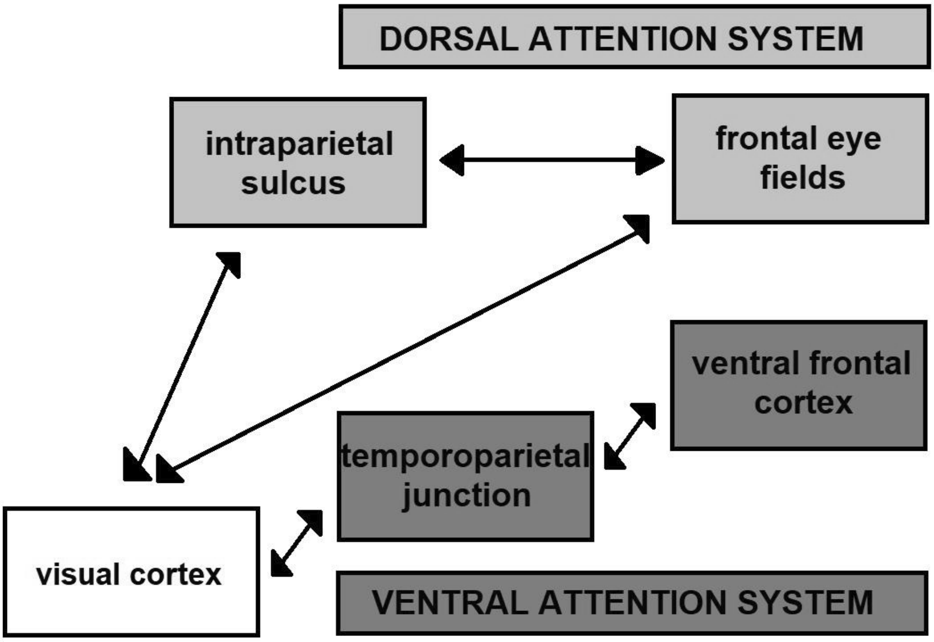


Figure 1 A simplified demonstration of the dorsal (light gray) and ventral (dark gray) visual attention systems (modified from the illustration by Vossel et al., 2014).

Brain imaging studies have brought evidence of the right hemisphere's dominance in both networks related to the spatial and nonspatial aspects of attention, as well as their interconnection (for a review, see Robertson, 2001). Specifically, the right temporoparietal junction is supposed to play a role in both of these aspects of attention (Robertson, 2001). According to an overview by Bellgrove and colleagues (2004), sustained and spatial attention networks may be partially interconnected: the right hemisphere includes sustained attention systems in the cortical regions, which may send activating input, via thalamic nuclei, to the brain-stem noradrenergic structures of *the alerting network*. These structures, in turn, may further provide input to the spatial attention systems of the parietal lobe (see also Petersen & Posner, 2012; Posner & Petersen, 1990).

1.3 NEGLECT

1.3.1 DEFINITION AND CLINICAL APPEARANCE

Neglect (i.e., *hemispatial* or *unilateral spatial neglect*) is a dramatic example of brain damage disturbing attention. The syndrome is by definition a failure to orient, report, or respond to stimuli located on the opposite side of a brain lesion (i.e., contralesionally), and which is not caused by sensory or motor defects (Heilman, 1979). The core deficit becomes evident as one orients toward the ipsilesional (i.e., the side on which the brain lesion is located) while simultaneously ignoring the contralesional space (Karnath & Rorden, 2012). The first descriptions of neglect are from the late 19th century, although the number of reports has increased considerably since the 1970s (Halligan & Marshall, 1993).

Neglect has major effects on patients’ everyday lives. The syndrome has been associated with sustained rehabilitation periods and weak outcomes when returning to independent living, and also has been linked to an elevated risk of falling injuries (Bartolomeo, 2007; Gillen et al., 2005; Jehkonen et al., 2000; Jehkonen et al., 2001; Katz et al., 1999; Malhotra et al., 2006; Paolucci et al., 1996; Paolucci et al., 1998; Ugur et al., 2000). Severe neglect becomes observable in everyday life, for example, by grooming, dressing, and eating only from the ipsilesional side, or by colliding into contralesional objects and humans. Neglect is a heterogeneous disorder containing several interrelated subtypes, which affects clinical appearance in addition to symptom severity. Table 1 presents common classifications of neglect subtypes, and their clinical manifestations.

In addition to contralesional deficits, neglect patients also show spatially nonlateralized (i.e., general) attention deficits (Bartolomeo & Chokron, 2002; Husain & Rorden, 2003; Robertson, 2001; Robertson et al., 1994). This becomes evident as impaired sustained attention (Robertson et al., 1997a), as well as selective attention (Chokron et al., 2019; Husain et al., 1997). Studies have demonstrated that severity of contralesional deficits correlates with difficulties in sustained attention (Robertson et al., 1997a). Neglect patients also show impairment in processing transient and small stimuli with flankers, as well as moving stimuli, in both visual fields (Battelli et al., 2001; Chokron et al., 2019; Duncan et al., 1999). These findings are clinically important because the presence of general inattention exacerbates contralesional deficits (Hjaltason et al., 1996; Husain & Rorden, 2003; Robertson, 2001; Robertson et al., 1997a; Samuelsson et al., 1998; van Kessel et al., 2010).

1.3.2 INCIDENCE AND RECOVERY

Neglect is a fairly common result of stroke, although incidence rates vary significantly, even between 12% and 95% in right-hemisphere stroke (Bowen et al., 1999; Robertson & Halligan, 1999). In a cohort study of Ringman and colleagues (2004; n = 1281), about 40% of patients suffering from stroke on the right hemisphere and 20% of patients suffering from stroke on the left hemisphere displayed the symptom in the acute phase. Neglect is reported not just more frequently, but also as being more severe and persistent after lesions in the right rather than the left hemisphere (Li & Malhotra, 2015; Mesulam, 1999; Ringman et al., 2004; although see Suchan et al., 2012). For acute neglect, recovery rates vary between 60% and 90% based on assessments made 3–12 months postinjury (Karnath et al., 2011). These figures have been questioned, however, insofar as the observed recovery is based on improvement in traditional tests (Bonato, 2012). Several studies (see e.g., Andres et al., 2019; Blini et al., 2016; Bonato et al., 2010; Bonato et al., 2012; Deouell et al., 2005; List et al., 2008; Rengachary et al., 2009) have demonstrated that in chronic phase neglect can be compensated in conventional tests, even though these apparently recovered patients show significant contralesional inattention in more demanding tasks.

Table 1 Neglect subtypes and their clinical manifestation.

SUBTYPE OF NEGLECT	CLINICAL MANIFESTATION
sensory neglect[a]	
	inattention or impaired awareness of the contralesional
visual	visual stimuli
auditory	auditory stimuli
somatosensory	tactile (i.e., touch), thermal, or painful (e.g., hot) stimuli
olfactory	failure to report the scents delivered to contralesional nostril
motor neglect[a]	reduced spontaneous use of the contralesional limb during motor activities
premotor neglect or directional hypokinesia[a]	impaired moving of head, eyes, or ipsilesional limb toward the contralesional hemispace
neglect in different frames of reference[b]	
egocentric neglect body-centered frames of reference	*viewer-centered* : impaired awareness of the contralesional side of space defined by the viewer's own eyes, head, or body
allocentric neglect environmental frames of reference	*stimulus-centered* : impaired awareness of the contralesional side of each individual stimulus regardless of its horizontal location in space *object-centered* : impaired awareness of the contralesional (e.g., left) side of objects with inherent left and right sides, such as words and maps (e.g., even if the inherent left side was located on the viewer's right side due to an upside-down position)
neglect in different regions of space[a,c]	
personal neglect	impaired perception and awareness of the side of the body contralesional to the brain damage
peripersonal neglect	inattention or impaired awareness of near space (within arm's reach) contralesional to the brain damage
extrapersonal neglect	inattention or impaired awareness of far space (beyond arm's reach) contralesional to the brain damage
representational or imaginal neglect[d]	impaired awareness of items in the contralesional space when recalling and describing imaginal details

[a]Kerkhoff, 2001; [b]Medina et al., 2009; [c]Caggiano & Jehkonen, 2018; [d]Heilman et al., 2000

1.3.3 CLINICAL CONDITIONS CO-OCCURRING WITH NEGLECT

There are several neuropsychological symptoms often co-occurring with neglect. One of these is *anosognosia*, a condition in which a patient is not aware of having an illness or symptom due to neurological disease (Grattan et al., 2018; Jehkonen et al., 2006; Starkstein et al., 1992). The condition is quite common after stroke, as the prevalence is about 30% (Jehkonen et al., 2006). Anosognosia predicts poor physical and functional outcome (Barker-Collo & Feigin, 2006; Jehkonen et al., 2000), and even milder deficits in symptom awareness may complicate recovery. Other conditions typically coexisting with neglect are hypoarousal and emotional indifference (Heilman et al., 1978). Neglect patients also show deficits in visuoconstructive skills and spatial working memory (Dupuy & Godefroy, 2007; Husain et al., 2001; Malhotra et al., 2003), as well as arithmetic processing (Mennemeier et al., 2004; Ricci et al., 2016; Robertson & Frasca, 1992). *Extinction* is a symptom characterized as the difficulty to attend to the more contralesionally located stimulus when two stimuli are simultaneously presented (Kerkhoff, 2001; Parton et al., 2004). It has been proposed that extinction would in fact be a subsymptom of neglect, or alternatively, that it would occur together with neglect (Brozzoli et al., 2006; Cohen, 2014; Husain, 2019). On the other hand, it has been indicated that these conditions may also double-dissociate, and differences have been reported in lesion locations (Cohen, 2014; Karnath & Rorden, 2012; Kerkhoff, 2001; Neppi-Modona, 1999).

1.3.4 THEORETICAL MODELS OF NEGLECT WITH RESPECT TO CLINICAL APPEARANCE AND BRAIN IMAGING FINDINGS

Research of neglect has brought a wide range of information, and theories, concerning attentional functions. According to one distinguished theory (Kinsbourne, 1970, 1993), both hemispheres account for functions directing attention to the contralesional hemispace. In the healthy brain, equilibrium is achieved by the two hemispheres inhibiting each other through interhemispheric connections. Unilateral brain damage results in disinhibition of the intact hemisphere and, as a consequence, in “hyperattention,” or exaggerated orienting, toward the ipsilesional space. Left hemisphere lesions cause milder neglect than lesions of the right hemisphere because an “unopposed” (disinhibited) orienting bias generated by the right hemisphere is weaker than the orienting bias of the left hemisphere (Kinsbourne, 1987). Another distinguished theory (Heilman & Van Den Abell, 1980; Mesulam, 1981, 1985, 1999) proposes that the direction of attention in space would be dominated by the right hemisphere, and this would explain why neglect typically occurs in patients who suffer from brain damage to the right hemisphere. Whereas the left hemisphere is involved in attention directed toward stimuli in the contralateral (i.e., right) hemispace, the right hemisphere is involved in the direction of attention toward both hemispaces. It has also been suggested that, in general, the right hemisphere might be more active and would process sensory information more efficiently than the left hemisphere in all attentional tasks (Mesulam, 1981). Therefore, left hemisphere damage would trigger a response where the right hemisphere ensures that resulting attention deficits are compensated for. However, after similar damage is sustained in the right hemisphere, no such compensation would occur, as the intact left hemisphere would continue to guide orienting only in relation to the right hemispace. According to a more pervasive theory (Mesulam, 1999), neglect may be a “network syndrome”—a collective and interactive outcome of multiple impairments in arousal, orientation, representation, and intention (see also Heilman et al., 1993; Mesulam, 1981).

Neglect has most frequently been associated with right-hemisphere stroke affecting the middle cerebral artery (Li & Malhotra, 2015) as well as various areas in temporal, parietal, and frontal lobes (Halligan et al., 2003; Mort et al., 2003; Ringman et al., 2004; Verdon et al., 2010). As neglect is a much-studied heterogeneous syndrome, research concerning brain imaging findings is varied and sometimes contradictory (Baldassarre et al., 2014; Karnath et al., 2011; Lunven et al., 2015; Saj et al., 2012). This may in part be attributable to the use of different imaging techniques, variations in the criteria used for diagnosing neglect, and whether the patients are studied in the acute or the chronic phase (Caggiano & Jehkonen, 2018; Karnath & Rorden, 2012; Li & Malhotra, 2015). There is also evidence of different aspects and subtypes of neglect being associated with lesions in different anatomical areas (Chechlacz et al., 2012; Hillis et al., 2005; Khurshid et al., 2012; Medina et al., 2009; Verdon et al., 2010).

Verdon and colleagues (2010) investigated the neural basis of neglect components by coupling a factorial analysis with a voxel-by-voxel lesion analysis. Eighty patients diagnosed with right-hemisphere stroke underwent neglect assessment with several tests as well as magnetic resonance imaging (MRI) of the brain. The study identified three main factors, which explained 82% of the total variance across the neglect tests: 1) perceptive/visuospatial, 2) exploratory/visuomotor, and 3) allocentric/object-centered components. Lesion–symptom mapping indicated that damage suffered in the right inferior parietal lobule had the strongest association with the perceptive and visuospatial aspects, whereas the right dorsolateral prefrontal cortex was similarly associated with the exploratory and visuomotor component. Deep temporal lobe regions in turn were linked to the allocentric or object-centered neglect component. Subcortical damage to paraventricular white-matter tracts correlated to severe neglect that covers multiple components.

Karnath and Rorden (2012), in turn, reviewed several structural brain imaging studies, and identified three main components for the core deficit of neglect. Their study indicated that the cortical areas most closely associated with neglect are the temporoparietal junction and inferior parietal lobule, the superior/middle temporal cortex and underlying insula, and the ventrolateral prefrontal cortex. Their study found that these same areas were involved irrespective of the lesion site (Karnath & Rorden, 2012; Suchan & Karnath, 2011). Authors proposed “the perisylvian neural network” interconnecting the aforementioned cortical areas, and representing the anatomical basis for the core deficit exhibited in neglect (Karnath, 2009; Karnath & Rorden, 2012; Wiesen et al., 2019). Lesions of several subcortical areas, for example, pallidum, putamen, caudate nucleus, pulvinar nuclei, and white-matter fiber tracts, have been also associated with neglect (Caplan et al., 1990; Karnath et al., 2002; Kumral et al., 1999; Wiesen et al., 2019). Interestingly, even such “subcortical neglects” have been linked to the perisylvian network; perfusion deficits of structurally intact perisylvian networks are evident in neglect patients with subcortical damage, but not in non-neglect patients with subcortical damage, suggesting that subcortical neglect is related to dysfunction of the cortical structures connected to the damaged subcortical area (Fruhmann Berger et al., 2009; Hillis et al., 2002, 2005; Karnath et al., 2005; Karnath & Rorden, 2012; Li & Malhotra, 2015).

1.3.5 ASSESSMENT OF VISUAL NEGLECT

Traditionally, neglect has been diagnosed by using paper-and-pencil (PnP) tests, as well as direct observation or scales (e.g., Catherine Bergego Scale; Azouvi et al., 1996; Bergego et al., 1995) that assess patients’ behavior in real-life situations (Kortte & Hillis, 2009; Robertson & Halligan, 1999). The first demonstrations on how neglect can be seen in simple copying, drawing, and pointing tasks are from the 1940s and 1950s (Halligan & Marshall, 1993; McFie et al., 1950). Subsequently, several PnP tests, such as various versions of the cancellation task, line bisection and figure drawing tasks, as well as text reading have been developed and they are still in wide-range use (Albert, 1973; Broeren et al., 2007; Funk et al., 2010; Ko et al., 2008; Schenkenberg et al., 1980; Seki et al., 2010; Tanaka et al., 2010; Verdon et al., 2010). Table 2 presents common clinical methods utilized in assessing visual neglect.

Different kinds of tasks typically bring out different aspects of neglect; for example, egocentric neglect can be seen in cancellation tasks, allocentric neglect in the line bisection test, and object-centered neglect in drawing tasks (Kerkhoff, 2001). This is only a broad classification, however, as one particular test can uncover various aspects of neglect. There are, for example, cancellation tasks that also reveal allocentric neglect (Ota et al., 2001). Most of the PnP tests assess neglect in peripersonal space. In addition to single tasks, comprehensive test batteries have been developed [e.g., Behavioral Inattention Test (BIT) by Wilson et al., 1987], as studies have indicated that a battery is more sensitive in assessing neglect than a single task alone is (Azouvi et al., 2002, 2006; Halligan et al., 1989).

Table 2 Common clinical methods used in assessing visual neglect.

CLINICAL ASSESSMENT METHOD	DESCRIPTION
Observation[a]	Neglect can be assessed by observing the patient's behavior: neglect patient may, e.g., eat only from the ipsilesional side of plate or collide into furniture on the contralesional side while moving.
Drawing tasks[a]	Patient is asked to draw an object, which is symmetrical from the left and right sides (e.g., clock or flower). Neglect patient's drawing is typically incomplete on the contralesional side.
Visual search (i.e., cancellation) tasks[a,b]	Patient is asked to search and to cross out targets (e.g., figures) presented on a paper sheet. Usually targets are placed among distractor figures and all figures are presented either in a random array or in lines. Neglect patient typically omits targets on the contralesional side of the sheet. The Bells Test[b] is one of the classical cancellation tasks. According to traditional criteria, neglect is diagnosed if the patient shows six or more contralesional omissions in this test.
Line bisection test[a,c]	Patient is asked to bisect horizontal lines. Neglect patient's mark in the task is typically biased toward the ipsilesional side, thus leaving the contralesional part of the line longer than the ipsilesional part.
Reading tests[a]	Patient is asked to read aloud a text. Neglect patient typically misses words placed on the contralesional side (e.g., close to the left marigin).
The Behavioral Inattention Test[a,d]	A test battery for the assessment of visual neglect. Contains traditional paper-and-pencil subtests (e.g., cancellation and line bisection tests), but also ecologically valid tasks, such as telephone dialing, coin sorting, and map navigating.

[a] Spikman & van Zomeren, 2010; [b] Gauthier et al., 1989; [c] Marshall & Halligan, 1990; [d] Wilson et al., 1987, Finnish version: Jehkonen, 2002

Severe neglect becomes easily evident in PnP tests, and in difficulties encountered in daily life (Gillen et al., 2005; Katz et al., 1999). Mild symptoms are more demanding to diagnose but they can also cause significant real-life problems (Bonato et al., 2012; Jehkonen et al., 2000). Several attempts have been made to increase the sensitivity of PnP tests in order to reveal mild neglect. Cancellation tasks, which are among the most widely used PnP tests, are considered very sensitive (Azouvi et al., 2002; Bowen et al., 1999; Ferber & Karnath, 2001, Halligan et al., 1991; Parton et al., 2004). Their sensitivity has further grown through an increment in the applied task demands, such as asking to perform the task while simultaneously counting backward (Robertson & Frasca, 1992), increasing the amount and similarity of target and distraction stimuli (Aglioti et al., 1997; Basagni et al., 2017; Bickerton et al., 2011; Chatterjee et al., 1999; Rapcsak et al., 1989; Sarri et al., 2009; Ten Brink et al., 2020), and using time limits for cancellation (Priftis et al., 2019). Sensitivity has also grown by calculating additional indices along with contralesional omissions. These include starting-point analyses (Azouvi et al., 2002; Nurmi et al., 2010; Nurmi et al., 2018), which bring out neglect patients' (atypical) tendency to start cancellation from the ipsilesional hemispace (Karnath, 1988; Kinsbourne, 1987; Olk et al., 2002).

Despite the aforementioned efforts, several studies (Bonato & Deouell, 2013; Deouell et al., 2005; Kim et al., 2010; Tanaka et al., 2005; Tsirlin et al., 2009; Ulm et al., 2013; van Kessel et al., 2010, 2013) have found that PnP tests are not sufficiently sensitive in detecting subtle neglect—even if attempts are made to improve the tests by introducing measures known to increase sensitivity (Bonato et al., 2012). Growing evidence on studies with right- (Bartolomeo, 2000; Bonato, 2015; Bonato et al., 2012; Bonato et al., 2013; Deouell et al., 2005; Eramudugolla et al., 2010; Smania et al., 1998; van Kessel et al., 2013) and left-hemisphere stroke patients (Blini et al., 2016; Bonato et al., 2010) suggest that an increment in attentional demands, and complexity of task, increases sensitivity in detecting subtle neglect (Blini et al., 2016; Bonato, 2012, 2015; Bonato et al., 2010; Hasegawa et al., 2011; Robertson & Manly, 2004). Computer methods offer several benefits over traditional ones. These include the possibility of observing a continuous measure such as reaction time (RT) to enhance precision, and modifying task demands to prevent compensatory effects (Bonato & Deouell 2013; see also Bartolomeo, 2000; Humphreys et al., 1996). Computer methods easily allow attentionally demanding settings, in which brief, dynamic, and concurrent stimuli are presented with the requirement of dividing attention (Bonato et al., 2010; van Kessel et al., 2010; van Kessel et al., 2013). A computer dual-task setting, in which two concurrent tasks are performed, and brief lateralized targets are presented, appears to be particularly effective in enhancing attentional requirements and task sensitivity (Andres et al., 2019; Blini et al., 2016; Bonato et al., 2010). Not surprisingly then, patients who appear intact even in the most demanding PnP tasks exhibit contralesional omissions in demanding computer tasks (Andres et al., 2019; Blini et al., 2016; Bonato et al., 2010, 2012; Deouell et al., 2005; List et al., 2008; Rengachary et al., 2009).

A significant body of research has compared new computer methods with PnP tests (e.g., Deouell et al., 2005; Kim et al., 2010; Tanaka et al., 2005; Ulm et al., 2013; van Kessel et al., 2010), and computer dual tasks have been similarly compared with single tasks (Andres et al., 2019; Blini et al., 2016; Bonato, 2015; Bonato et al., 2010, 2012; van Kessel et al., 2013). However, to my knowledge, no study has made comparisons among qualitatively different computer methods. Additional research is needed because there are contradictions in past findings on visuoattentive deficits in unilateral stroke patients. Possibly, due to methodological variations, studies have found either 1) prominent contralesional but not ipsilesional inattention (Bonato, 2015; Bonato et al., 2012), 2) mild ipsilesional inattention coupled with notable contralesional inattention (Bonato et al., 2019; Chokron et al., 2019), or even 3) considerable ipsilesional inattention at the absence of contralesional inattention (Robertson et al., 1994; Williamson et al., 2018). There are also limitations regarding the research on general and lateralized inattention, and their associations, in unilateral stroke patients. Some studies that found general but not lateralized inattention had either ruled out the neglect syndrome with a single PnP method (Rueckert & Grafman, 1998), or they had not evaluated the syndrome's existence at all (Rueckert & Grafman, 1996; Wilkins et al., 1987). In contrast, other studies associating general and lateralized inattention have been successful in diagnosing clear neglect with PnP methods (Chokron et al., 2019; Robertson et al., 1997a; Robertson et al., 1998). Therefore, possible associations with *subtle* lateralized and general inattention remains elusive, when the inadequacy of PnP methods in assessing and diagnosing mild neglect is taken into account (Bonato, 2015; Bonato & Deouell, 2013; Bonato et al., 2012; Buxbaum et al., 2004; Deouell et al., 2005; Kim et al., 2010; Ogourtsova et al., 2017; Peskine et al., 2011).

Finally, there is also some criticism concerning basic computer applications, because they introduce stimuli in a narrow visual view (Ulm et al., 2013). Tasks displayed on standard, relatively small-screen devices, or on small-sized (e.g., letter-sized) paper, may be lacking in ecological validity (Bonato & Deouell, 2013; Hasegawa et al., 2011; Nakatani et al., 2013; Ulm et al., 2013). Thus, applications utilizing large perceptual space might enhance sensitivity and ecological validity of the assessment of visuoattentive deficits.

2 AIMS OF THE PRESENT STUDY

The aim of the present set of studies was to investigate whether visuoattentive deficits of unilateral stroke patients could sensitively be revealed with computer-based methods. To answer the study questions, a novel large-screen computer method was developed, and another relatively recent computer test-battery was used.

The specific objectives were the following:

1 to examine whether varying the complexity of the large-screen dual task would improve the sensitivity of the assessment and enable the identification of subtle visual neglect (Study I);

2 to compare contralesional and general visuoattentive deficits between left- and right-hemisphere stroke patients by utilizing two computer methods with different characteristics (Study II);

3 to investigate whether signs of visual neglect can be sensitively uncovered with a computer cancellation task presented on a large screen, or with attentionally demanding dual tasks presented on a standard computer screen (Study III).

3 METHODS

3.1 PARTICIPANTS

Participants were recruited and data was collected in the timeframe of June 2016 to February 2019. All participants were native Finnish-speaking adults. Patient participants were selected from a group of 58 potentially suitable consecutive stroke patients who were all undergoing rehabilitation at the Neurology Outpatient Clinic of Helsinki University Hospital (HUH). All patients underwent brain imaging for clinical purposes during the acute phase of stroke. Patients with first-ever stroke verified with computed tomography (CT) or MRI were included while the following exclusion criteria were observed: prior neurological diagnosis with an adverse effect on cognition, stroke affecting both hemispheres, any visual-field deficit diagnosed either in a clinical neurological or neuro-ophthalmological evaluation, primary auditory or visual impairment (except for myopia or hyperopia, which had been adequately addressed with glasses), severe aphasia or any other severe cognitive symptom preventing participation, substantial motor symptoms, severe diagnosed psychiatric disease, or substance abuse that complicated cooperation. All in all, 18 patients were excluded due to prior stroke, stroke affecting both hemispheres, visual-field deficit, or severe neglect that prevented necessary cooperation. The final sample consisted of 20 left-hemisphere stroke (LHS) patients, 20 right-hemisphere stroke (RHS) patients, and 20 controls recruited from among healthy volunteers. The demographic and clinical characteristics of the participants are laid out in Table 3, and related details of the assessment methods in Section 3.4.1.

3.2 ETHICAL ASPECTS

The patients' clinical care and rehabilitation were conducted according to HUH standards and guidelines. All participants received comprehensive verbal and written information regarding the study and gave their written informed consent for participation. The study was approved by the Department of Neurology, and the Ethics committee of HUH. Research procedures were conducted in compliance with the Helsinki Declaration.

3.3 PROCEDURE

Each participant went through a neuropsychological examination with a structured interview and also performed seven computer-based tasks: four large-screen tasks and three other computer tasks. The computer tasks were always performed in the same order: the large-screen tasks were performed first, followed by the other computer tasks. All studies were conducted according to a written study protocol.

Controls performed the neuropsychological examination and the computer tasks in the same session, with identical presentation orders. Patients performed all computer tasks in one session, with fixed order, but neuropsychological examinations were conducted as a part of the clinical evaluation at the beginning of the rehabilitation period.

3.4 ASSESSMENT METHODS

3.4.1 COLLECTION OF PARTICIPANT CHARACTERISTICS AND NEUROPSYCHOLOGICAL EXAMINATION

Participant characteristics (Table 3) were collected by utilizing a structured interview, HUH medical records, and questionnaires assessing depressive symptoms, alcohol consumption, and subjective cognitive and emotional symptoms. The neuropsychological examination included several cognitive tests assessing visual attention, executive functions, processing speed, and memory. Visual inattention was assessed with the Bells Test (Gauthier et al., 1989) and the Twinkle Task (a novel method; see Section 3.4.2.5.). A number of tests were used to examine executive functions and processing speed. These were the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997), Parts A and B of the Trail Making Test (TM A and TM B; Reitan, 1958), the design, phonetic, and semantic fluency tests (Jones-Gotman & Milner, 1977; Miller, 1984), and the Bourdon–Wiersma Test (B-W), which was incorporated with a dual-task setting (Vilkki et al., 1996). These tests include varied requirements for the participants. For example, TM A and TM B require visual scanning, whereas TM B also requires set shifting. The design, phonetic, and semantic fluency tests require producing figures or words belonging to a designated category. The B-W dual task requires participants to count numbers backward while simultaneously cancelling visual dots. Memory functions were assessed utilizing subtests of the Wechsler Memory Scale, third edition (WMS-III): Letter-Number Sequencing and Visual Memory Span (Wechsler, 1997, 2008), together with a working-memory distraction task, word-list learning, and delayed recall of the wordlist (Christensen, 1979). The working-memory distraction task includes a heterogenous and homogenous interference subtasks. In the heterogenous interference subtask, participants were asked to first repeat a group of three words, then to perform a mental-arithmetic task, and finally to recall the words. In the homogenous interference subtask, participants were asked to first repeat two three-word groups, and then to immediately recall the words. Both of the subtasks were performed two consecutive times. The word-list learning task contained ten words with four learning trials. In delayed recall, participants were asked to recall the wordlist after a 30-min delay. Detailed questionnaires and neuropsychological tests are presented in Table 4.

Table 3 Demographic and clinical details of the participant groups.

Demographic and clinical variables	LHS patients N = 20	RHS patients N = 20	Controls N = 20	Statistics	df	*P* value[c]	Effect size[d]
RHS patients vs. LHS patients vs. Controls							
Age; years[a]	51 (9)	53 (8)	46 (15)	$\chi^2 = 2.375$	2	.305	
Gender; female / male[b]	25% / 75%	55% / 45%	60% / 40%	$\chi^2 = 5.759$	2	.056	
Handedness; left / right[b]	0% / 100%	5% / 95%	0% / 100%	$\chi^2 = 2.034$	2	.362	
Education; years[a]	16 (4)	15 (3)	16 (3)	$\chi^2 = 0.390$	2	.823	
DEPS score[a,1]	5 (4)	5 (4)	3 (4)	$\chi^2 = 4.158$	2	.125	
AUDIT score[a,e,1]	6 (5)	7 (6)	5 (3)	$\chi^2 = 0.017$	2	.991	
RHS patients vs. LHS patients							
CLCE-24 score[a,e,1]	58 (7)	60 (4)		*U* = 170.5; Z = -.801	1	.423	
Lesion type; hemorrhagic / ischemic / both[b]	5% / 90% / 5%	15% / 60% / 25%		$\chi^2 = 4.867$	2	.088	
Days postonset of stroke prior to study[a]	105 (42)	106 (45)		U = 199.5; Z = -.014	1	.989	
Outpatient rehabilitation sessions prior to study[a]	3 (2)	3 (2)		*U* = 186.5; Z = -.369	1	.712	
Type of outpatient rehabilitation[b,2]	50% / 50%	70% / 30%		$\chi^2 = 1.667$	1	.197	
Visual neglect at the early stage of recovery during ward care[b,3]	15%	55%		$\chi^2 = 7.033$	1	**.008**	φ = .419**

[a] Mean (standard deviation); Kruskal-Wallis or Mann–Whitney U Tests (χ^2 / U); [b] Percentage; Pearson Chi-Square Test (χ^2); [c] *P* values smaller than .05 are statistically significant (marked in bold)
[d] Effect sizes according to Cohen (1988): φ = *small >.1, **medium >.3, ***large >.5; effect sizes given for significant group differences
[e] Unpublished analyses; rest of the data presented in Studies I and III; [1] Details of the questionnaires are presented in Table 4; [2] Multiprofessional rehabilitation / only neuropsychological rehabilitation
[3] Based on clinical neuropsychological examination carried out 13 (SD 15) days poststroke; LHS = left hemisphere stroke; RHS = right hemisphere stroke; df = degrees of freedom
DEPS = Depression scale; AUDIT = Alcohol use disorders identification test; CLCE = Checklist for cognitive and emotional consequences following stroke

Table 4 Self-reporting questionnaires and neuropsychological tests used in the study.

Self-reporting questionnaires

Depression scale, DEPS[a]	questionnaire consists of 10 items with total scores ranging from 0 to 30; the lower the score the less severe the symptoms
Alcohol use disorders identification test, AUDIT[b]	questionnaire consists of 10 items with total scores ranging from 0 to 40; the lower the score the less the consumption
Checklist for cognitive and emotional consequences following stroke, CLCE-24[c,1]	questionnaire consists of 22 cognitive or emotional problems; in the present study 1–3 points for each problem: hindering life severely (1p), mildly (2p), not at all (3p); total score ranging from 22 to 66; the lower the score the more severe the symptoms

Neuropsychological tests

VISUAL ATTENTION
- Bells Test[d]
- Twinkle Task[e]

MEMORY
- WMS-III[f]
  - WMS-III Letter-Number Sequencing
  - WMS-III Visual Memory Span
- Working-memory distraction task, list learning, and delayed recall[g]
  - Verbal working-memory distraction task with heterogenous (numeric) and homogenous (verbal) interference subtask
  - Word-list learning of ten words with four learning trials
  - Delayed recall of the wordlist

EXECUTIVE FUNCTIONS AND PROCESSING SPEED
- Trail Making Test, Parts A and B[h]
- Brixton Spatial Anticipation Test[i]
- Fluency[j]
  - Phonetic fluency
  - Semantic fluency
  - Design fluency
- B-W, dual-task modification[k]
  - B-W number count (single task)
  - B-W dot cancellation (single task)
  - B-W number count (dual task)
  - B-W dot cancellation (dual task)

[a]Salokangas et al., 1995; [b]Saunders et al., 1993; [c]van Heugten et al., 2007; [d]Gauthier et al., 1989; [e]a novel cancellation task; [f]Wechsler, 1997, 2008; [g]Christensen, 1979; [h]Reitan, 1958; [i]Burgess & Shallice, 1997; [j]Jones-Gotman & Milner, 1977, and Miller, 1984; [k]Vilkki et al., 1996

[1] "Don't know" responses were replaced with an average response of each patient in question (6% of all responses in the LHS group and 3% in the RHS group)

B-W = Bourdon–Wiersma; WMS-III = Wechsler Memory Scale, third edition; LHS = left hemisphere stroke; RHS = right hemisphere stroke

3.4.2 LARGE-SCREEN COMPUTER TASKS

3.4.2.1 APPARATUS

The Active Space, a novel large-screen computer method, was designed and constructed as an application of a previously developed device using near-field imaging technology (Linnavuo et al., 2010; Rimminen et al., 2010). In the Active Space, a short-throw video projector (Epson EB-680, Seiko EPSON Corporation, Suwa, Japan) was utilized to project visual stimuli on a wall. The wall size of the display was 277 × 173 cm and the central point of the display was located 120 cm above floor level. The viewing distance was 180 cm, which translates to a display extending about 75° horizontally and 51° vertically, with pixels appearing 1.9 × 1.9 mm in size. LabVIEW™ systems engineering software (National Instruments, Austin, Texas, USA) was used to control the test protocol and the tasks presented on the large screen in this method.

In the large-screen research setting, participants performed the tasks seated. A short briefing and practice trial preceded each task. The presentation order was fixed: 1) the Ball Rain Task, 2) the Detection Task, 3) the Crash Task, and 4) the Twinkle Task.

3.4.2.2 BALL RAIN TASK

Stimuli. Nonoverlapping spheres (diameter 100 mm) with different colors appeared from the top of a display and moved rapidly downward (velocity 1.1 m/s). The appearing of the spheres was random (interstimulus interval, ISI, 0–750 ms), and could occur in any horizontal location from the extreme left to the extreme right (Figure 2). The target was the red sphere [red, green, blue color-model triplet, RGB: (190,0,0)], introduced until response or 700 ms, which was set as the maximum display time. There were altogether 100 targets (50 on the left side and 50 on the right side of display) appearing randomly (intertarget interval, ITI, 1200–4900 ms). Spheres that were not red were used as distractors [display time 700 ms; colors: navy blue (0,0,100); blue (0,0,255); cyan (0,255,255); yellow (255,255,0); dark green (0,100,0); pine green (0,100,100); green (0,255,0); purple (100,0,100); pink (255,0,255)]. The background of the display was solid gray (127,127,127).

Research setting. Each participant was asked to observe the appearing spheres, and to respond by clicking mouse button 4 when detecting a red sphere. They were asked to ignore all other spheres. A task of 3 min was employed, and a 30-s training run was performed prior to commencing the task. RTs for correct responses and the number of omissions were automatically registered by the software. The response window was 250–1000 ms after target onset (for primary RT analyses, see Section 3.5.1). The Ball Rain Task is illustrated in Figure 2.

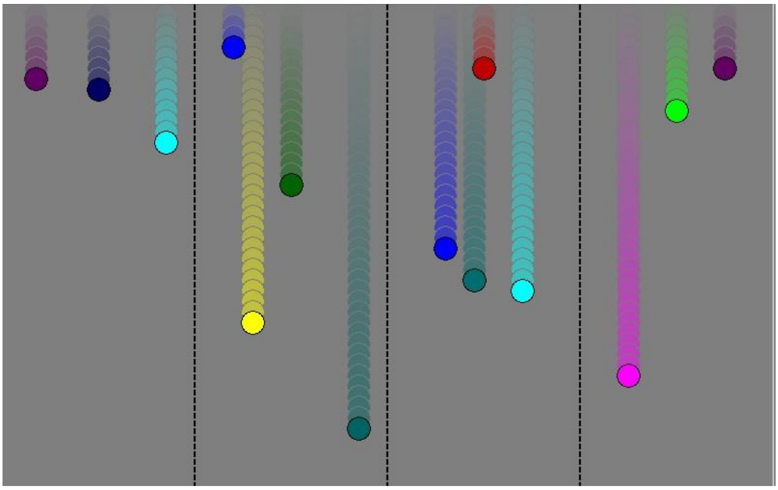


Figure 2 Schematic illustration of the Ball Rain Task. Red sphere (the target) is visible on the right side of the screen.

3.4.2.3 DETECTION TASK

The Detection Task is a visual dual task that utilizes a peripheral visual-field task as well as a numeric central task, both of which are presented simultaneously as a part of the dual-task paradigm.

Peripheral task. Colored spheres (diameter 100 mm) flashed briefly (100 ms), and randomly (ISI 1.5±1.5 s), one at a time in various locations of the display. A red sphere [RGB: (190,0,0)] was the target, whereas spheres with other colors [green (0,255,0); blue (0,0,255); cyan (0,255,255); yellow (255,255,0)] were distractors. In total, 20 targets were generated (10 on the left and 10 on the right side of the display) by flashing at random intervals (ITI 6.3±3.8 s) in random vertical positions. The background of the display was solid gray (127,127,127).

Central task. Varying numbers appeared and constantly changed in the center of the display (0–3 in random order; height 50 mm; presentation 800 ms; ISI 1 s). Number 2 was the target and appeared randomly (ITI 6.5±4.5 s).

Procedure. In the peripheral task, participants were required to observe flashing spheres, and to respond to every red sphere by clicking on mouse button 4. In the central task, they were asked to observe the central numbers, and to respond to the number 2 by clicking button 4 on the mouse. The peripheral and central tasks were performed simultaneously but the targets of the peripheral and central tasks never appeared concurrently (of which the participant was not informed). Before the actual 2-min test, each participant was given time to perform three 30-s practice trials: first the peripheral and central tasks were trained separately and then, in the third practice run, simultaneously. RTs for correct responses and the number of missed targets were registered by the software. Only responses to the peripheral targets were analyzed. The response window was 250–1000 ms after target onset (for primary RT analyses, see Section 3.5.1.). The Detection Task is illustrated in Figure 3.

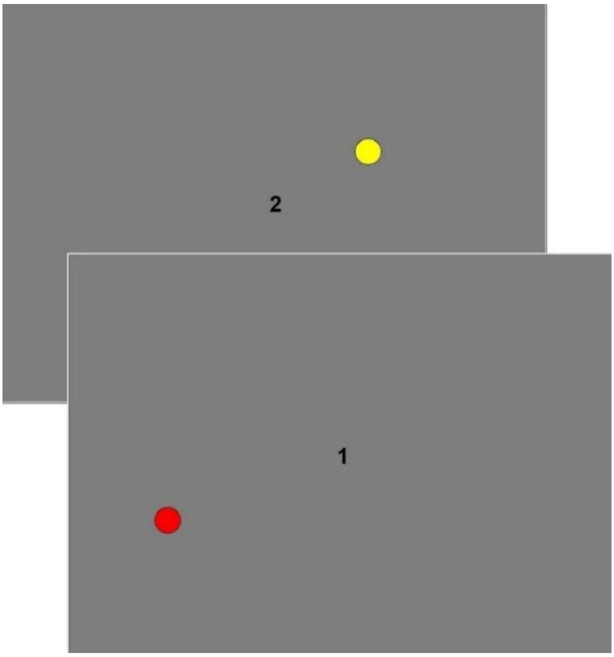


Figure 3 Schematic illustration of the Detection dual task. Central target (2) appearing on top, and peripheral target (red sphere) on bottom.

3.4.2.4 CRASH TASK

Similar to the Detection Task, the Crash Task is a visual dual task that relies on the simultaneous presentation of a peripheral visual-field task and a numeric central task. The Crash Task was designed to be more complex than the Detection Task. To achieve this, 1) demands for arithmetic processing required for the central task were increased, 2) different responses to central and peripheral targets were required, 3) duration of the task was doubled, and 4) salience of the targets was decreased.

Peripheral task. Gray spheres [RGB: (127,127,127); diameter 90 mm] appeared from random locations of the four margins of the display and moved across the screen. Two spheres would collide randomly (ITI 6.6±5 s), resulting in a flash (100 ms) of a white sphere [the target; diameter 240 mm; RGB: (255,255,255)]. There were 48 targets (24 on either side of the screen, with random vertical location and sequence). The background of the display was gray noise.

Central task. Varying and constantly changing numbers (1–9 in random sequence; height 245 mm; display time 800 ms; ISI 1.5 s) were generated onto the middle of the display. The target appearing randomly (ITI 10±5 s) was any number that was twice as large as the preceding number.

Procedure. In the peripheral task, participants were asked to observe the moving spheres, and to respond to each collision (resulting in a white flash) by clicking button 4 on the mouse. The central task consisted of an arithmetic assignment in which participants were required to observe changing digits, and to react every time a number appeared that was equal to 2 times the immediately preceding one (alternatives: 1→2, 2→4, 3→6, 4→8). Responses were given by saying “hep,” which was captured on a lavalier microphone. The Crash Task required simultaneous performing of the peripheral and central tasks as a dual task. However, the peripheral and central targets did not appear simultaneously (of which the participant was not informed). Task duration was 4 min, and prior to undertaking the task the participants underwent three 30-s practice trials: First the peripheral and central tasks were both practiced separately, and in the third trial they were combined as a dual task for a final practice run. RTs for correct responses, and any missed targets, were registered. Only RTs and omission errors for peripheral targets were analyzed. The response window was 250–1500 ms after target onset (for primary RT analyses, see section 3.5.1). The Crash Task is illustrated in Figure 4.

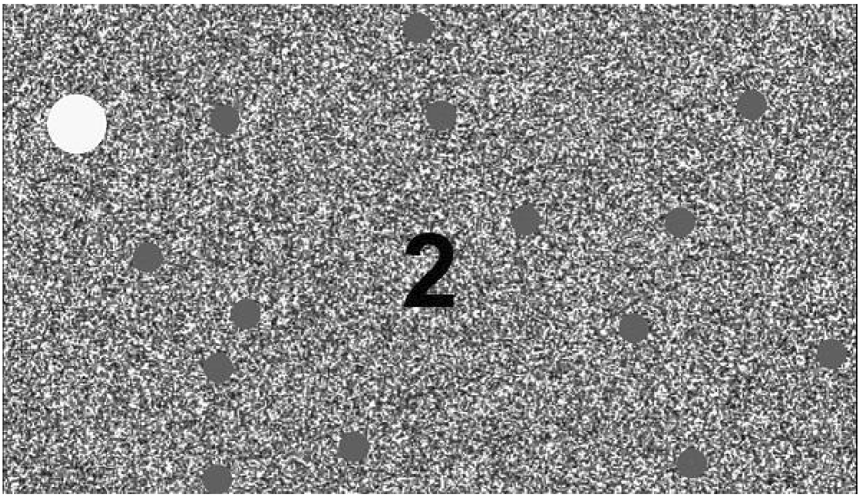


Figure 4 Demonstration of the Crash dual task. Peripheral target (white flashing sphere) appearing on the left side of the display.

3.4.2.5 TWINKLE TASK

The Twinkle Task was developed by adopting the original ideas of Wilson and colleagues (1987) and Ota and colleagues (2001). Wilson and collaborators presented a Star Cancellation PnP task as a segment of the Behavioral Inattention Test (BIT) battery designed to assess visual neglect. The task utilizes a sheet filled with scattered letters, words, and five-point stars of two different sizes placed on random positions. The participant is tasked with selecting the small stars. Ota and colleagues designed two discriminative PnP cancellation tasks, one utilizing circles and the other, triangles, with the intention of enabling the dissociation of allocentric and egocentric neglect. Both tasks contain complete and incomplete figures (circles or triangles, respectively). Participants would be given instructions to circle all intact figures and to cross out all incomplete figures. Incomplete figures would be missing a portion ("the gap") on either side. Other gap cancellation PnP tasks have also been developed (Bickerton et al., 2011; Chechlacz et al., 2010; Demeyere et al., 2015; Mancuso et al., 2015; Parton et al., 2006).

Task. The Twinkle Task contains 180 five-pointed, equal-sized stars arranged in a random manner. There are 70 incomplete stars (the targets), with an open cut end at one point of the star (the gap), and 110 complete stars (the distractors). Thirty-one of the targets are positioned on the left, 31 on the right, and 8 in the central area (with these areas corresponding to 46%, 46%, and 8% of the whole field, respectively). Thirty of the targets had been altered so that they were missing a point on the left side, and 30 targets had been similarly edited and lacked a point on the right side, as well as 10 targets where the missing point was located either straight up or straight down. The Twinkle Task is illustrated in Figure 5.

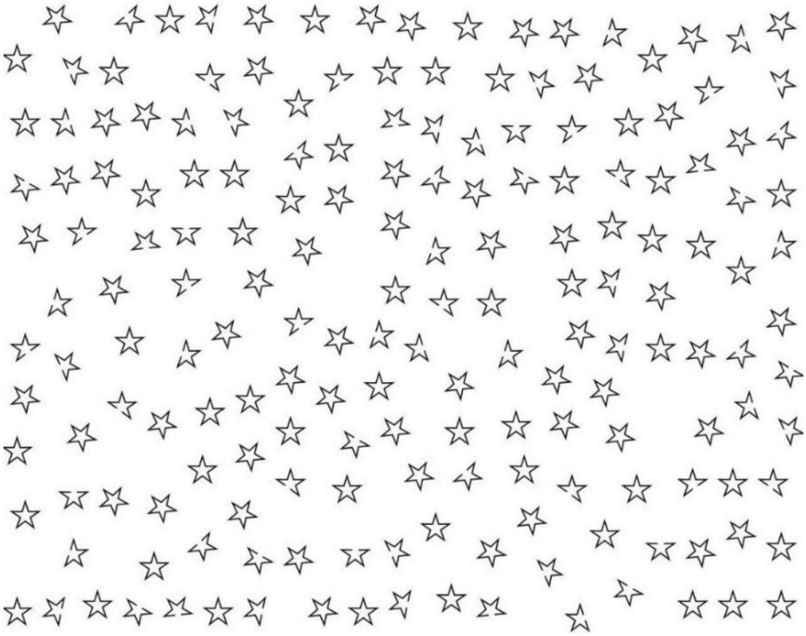


Figure 5 The Twinkle cancellation task, where the participants' task is to find the target stars missing one of the five points.

Two analogous media for the presentation of the Twinkle Task were applied. Participants completed the Twinkle Task in large-screen as well as PnP format, the latter of which was created by means of a simple screenshot of the large-screen test. Therefore, the two versions were identical except for the utilized media, as they incorporated the same stimuli, and their positioning and proportions remained in scale. To attempt to increase assessment sensitivity of the Twinkle Task, visuoperceptual demands were increased by incorporating parameters that led to high prevalence and low salience of the targets (see Figure 5). A time limit in the large-screen version was also used.

Large-screen setting. A task sheet was projected onto a 277 × 173 cm screen. The size of the display was 1280 horizontal and 1024 vertical pixels. The parameters for target locations were set so that the left-side limit for target occurrence was at 38 pixels and the right-side limit correspondingly at 1254 pixels. Each complete star extended 10 cm horizontally and vertically (about 1°) and target stars were of the same size except for the missing point. The participant was asked to observe the display, and to search and mark all of the targets. Target selection was completed by hovering a cursor over the target to be selected on the screen, and by subsequently clicking the left mouse button to complete the selection. All participants used their dominant hand to complete this task. After picking a target, a black cross appeared over the target. The answers were final, as they could not be cancelled afterward. The participants were not made aware of the number of targets and they were simply encouraged to accomplish the task as quickly as possible and, once completed, to immediately notify the experimenter who then stopped the task. The maximum performance time was 3 min, after which the task display disappeared automatically. Participants were informed about the time limit. A 30-s practice run, during which six targets were introduced in the central area of the display, was conducted prior to the actual test. Correct selections, omissions, performance time, and individual scanning patterns with all selections in chronological order registered on the computer.

PnP setting. The participant was seated and the sheet containing the task was presented in front of the participant on the desk. The sheet was A4 in size, and each complete star extended 8 mm horizontally and vertically, and the target stars were of the same size except for the missing point. The midline of the sheet was placed at the midline of the participant. The participant was instructed to cross out all of the targets as quickly as possible with a pen held in the dominant hand, and upon completing the task, to notify the experimenter who manually stopped the timer. No time limit was applied in the PnP setting.

3.4.3 OTHER COMPUTER TASKS

A computer-based test battery, developed by Bonato and colleagues (2010), was used and adjusted into Finnish. The paradigm was programmed and administered using E-Prime (Psychology Software Tools, Sharpsburg, Pennsylvania, USA, http://www.pstnet.com/). The test battery consisted of three separate conditions with similar stimulus presentation but different procedures.

For every condition, each individual participant was seated at a distance of about 60 cm from a 15” display. Each trial began with a blank white display being presented for 1000 ms, after which a black cross was introduced to the center of the display (central fixation, duration 1000 ms). Then, lateralized black target(s) in the shape of dot(s) (diameter 8 mm, flash time 50 ms) appeared 135 mm (12.8°) to the left or right from the center (unilateral targets) or concurrently at both sides (bilateral target). Simultaneously with the lateralized target(s), a central target in the form of a letter (*a*, *b*, *v*, or *z*; font size 38; duration 50 ms; location in the center of the display), together with an auditory stimulus in the form of a spoken number (“one,” “two,” “eight,” or “nine” in Finnish), were presented. One stimulus per type [dot(s), letter, number] appeared in each trial. Altogether, 48 trials (16 randomized targets of each type) were presented.

The *Lateralized Targets Computer Task* (LTCT) required participants to verbally report on which side the dot target(s) were located (“left,” “right,” “both sides,” or “no response”) but to ignore the central stimulus (the letter) as well as the verbal stimulus (the spoken number).

The *Visual Dual Task* required a reaction to two stimuli types. Participants were required to first read aloud the central (letter) stimulus, and after that, similar to the LTCT, to verbally report on which side the dot target(s) were located, while still disregarding the verbal stimulus.

In the *Auditory Dual Task*, participants were again required to react to two stimuli. First, the participant was required to count aloud forward, twice, in increments of two starting from the spoken number stimulus (the correct reaction, e.g., to the number eight would therefore be to recite out loud: “8, 10, 12”), and then report on which side the dot target(s) were located. In this setting, the central (letter) stimulus was to be ignored.

Prior to each condition, the participants were given verbal instructions and the chance for a short practice trial. The participants’ verbal responses (i.e., the position where participants reported each target) were registered by the experimenter. No limitation was set for response times; a new target was never introduced prior to a reaction to the preceding one. After the visual stimuli presentation (50 ms), a noisy black-and-white screen appeared and remained onscreen until the following trial commenced.

In each condition, unilateral and bilateral trials were analyzed separately. An omission for a unilateral dot target was recorded whenever the participant did not correctly report the target position (“left” or “right”). In bilateral trials, “left omission” meant that the participant incorrectly responded with “right” when a target actually appeared on both sides (i.e., left-sided extinction). Accordingly, “right omission“ meant that the participant reported a bilateral target as being on the left, while in reality it appeared simultaneously on both sides (i.e., right-sided extinction).

Table 5 summarizes all of the computer-based tasks used in the study. The tasks are grouped according to domain (single vs. dual task) and the size of the test field (standard vs. large screen).

Table 5 Computer-based tasks used in the study.

	Standard screen	**Large screen**
Single domain	LTCT (Study 2)	Ball Rain Task (Study 2) Twinkle Task (Study 3)
Dual domain	Visual Dual Task (Study 3) Auditory Dual Task (Study 3)	Detection Task (Study 1) Crash Task (Study 1)

LTCT = Lateralized Targets Computer Task

3.5 DATA ANALYSIS

3.5.1 PRIMARY REACTION TIME ANALYSES

Primary RT analyses of the Ball Rain, the Detection, and the Crash Tasks were carried out adopting an approach similar to previous studies examining visual neglect (Anderson et al., 2000; Deouell et al., 2005). The target was recorded as “missed” if the response was not given within the allowed time window. The upper limit of the window was determined individually for each task, based on the shortest ITI (a response had to be given before the appearance of the next target). The following exclusions were also conducted: 1) Responses that were faster than 250 ms from target onset were construed as anticipatory errors and consequently excluded (the decision was based on a distribution of all responses within each task), and 2) RTs deviating more than 2.5 standard deviations (SDs) from the mean were considered outliers and consequently excluded. The exclusion criteria were applied independently for each task, participant, and hemifield, which led to the exclusion of a total of 3% of all responses in the Ball Rain and Crash Tasks, and 2% in the Detection Task.

3.5.2 STATISTICAL ANALYSES

Statistical analyses were conducted by using the SPSS (Version 25.0, IBM Corporation, Armonk, New York, USA). In all analyses, data was screened for normality, and the statistical significance level was set at .05.

3.5.2.1 VARIABLES AND ANALYSES OF DEMOGRAPHIC, CLINICAL, AND NEUROPSYCHOLOGICAL DATA

Variables of the demographic, clinical, and neuropsychological data are presented in Tables 3 and 6. Only nonparametric statistical methods were utilized in analyses because of skewed distributions of continuous variables. Group comparisons were conducted by using Mann–Whitney U (LHS patients vs. RHS patients) or Kruskal–Wallis (LHS patients vs. RHS patients vs. controls) Tests for continuous variables and the Pearson’s Chi-Square Test for categorical variables. For *post hoc* pairwise comparisons Dunn’s Test was used. For multiple comparisons, *P*-value adjustments were made with the Bonferroni correction.

3.5.2.2 VARIABLES AND ANALYSES OF THE COMPUTER METHODS, AND THE PNP CANCELLATION TASKS

Average RTs were determined separately for each participant, hemifield, and task. Analyses were carried out using a mixed ANOVA with *group* (LHS patients vs. RHS patients vs. controls) as a between-participants factor, and *hemifield* (left vs. right) as well as *task* (Detection vs. Crash; Study I) as within-participants factors. For multiple pairwise comparisons, *P*-value adjustments were made with the Bonferroni correction.

Because of skewed distributions, all the other variable analyses were conducted using nonparametric tests.

The proportion of *omissions* was calculated individually for each participant, hemifield, and task. Between-groups analyses (LHS patients vs. RHS patients vs. controls) were performed with the Kruskal–Wallis Test. *Post hoc* analyses were conducted with Dunn’s Test. For multiple pairwise comparisons, *P*-value adjustments were made with the Bonferroni correction (Studies I and III) or the step-down multiple hypotheses testing procedure (Benjamini & Liu, 1999; Study II). Within-group analyses (i.e., analyses on differences in omissions between the two hemifields) were conducted using paired Wilcoxon Signed–Rank Test.

Asymmetry indices (AIs; see, e.g., Blini et al., 2016) were determined in Study II to analyze spatial bias (contralesional deficits) in visual attention by subtracting left hemifield omissions from right hemifield omissions. Consequently, negative values of the AI indicated the left-sided omissions being dominant (which signifies attention deficits on the contralesional side in RHS patients), and positive AIs indicated that the right-sided omissions were dominant (which in turn signifies attention deficits on the contralesional side in LHS patients). Zero indicated the expected equality between the left-sided and right-sided omissions. AIs were determined separately for the Bells Test, and in the LTCT for both unilateral and bilateral trials. Between-groups analyses (LHS patients vs. RHS patients vs. controls) were carried out by using Kruskal–Wallis Test. For *post hoc* analyses, Dunn’s Test was used. To control the family-wise error, the step-down multiple hypotheses testing procedure was applied. Within-group analyses (the variation of the AIs from the expected zero) were performed using one sample Wilcoxon Signed–Rank Test.

In Study III, along with omission analyses, Mean Position of Hits (MPHs), starting points, and performance times were analyzed in order to attempt to increase assessment sensitivity of the new cancellation task. The decision was based on the findings of Study I; that is, on the fact that none of the patients exhibited symptoms of visual neglect in the Bells Test according to traditional criteria (the range of contralesional omissions for both patient groups in the Bells Test was 0–4).

MPH (Toraldo et al., 2017) is a standardized statistical method to analyze whether correctly selected targets are distributed asymmetrically across the cancellation task sheet. For each participant, an electronic image of the Twinkle Task sheet was used to create the numeric value of MPH; that is, the standardized value of the mean horizontal location (x coordinate in pixels) of correctly selected targets. The MPH varied from -0.5 (left) to +0.5 (right). Therefore, negative values indicate a leftward deviation from the mean (i.e., dominance of right-sided omissions), and correspondingly, positive values a rightward bias (i.e., dominance of left-sided omissions). Zero indicated that the selected targets were distributed equally across the test sheet. The differences between the groups (LHS patients vs. RHS patients vs. controls) in MPHs were analyzed using Kruskal–Wallis Test.

The *starting points* (SPs) of visual searching were determined for each participant for the large-screen Twinkle Task according to horizontal location (x coordinate in pixels) of the first target selected by each participant. The group differences (LHS patients vs. RHS patients vs. controls) were analyzed using Kruskal–Wallis Test.

Performance times were determined separately for each participant and each version of the Twinkle Task. For the present dissertation (i.e., unpublished data), performance times for the Bells Test were also analyzed. Between-groups analyses (LHS patients vs. RHS patients vs. controls) were carried out by using Kruskal–Wallis Test. Dunn's Test was used for *post hoc* analyses. For multiple pairwise comparisons, *P*-value adjustments were made with the Bonferroni correction. Within-group analyses (performance time differences between the large-screen and the PnP versions of the Twinkle Task) were performed using paired Wilcoxon Signed–Rank Test.

3.5.2.3 EFFECT SIZES

Effect sizes were computed by determining eta squared (η^2) for Kruskal–Wallis Test, r for Mann–Whitney U and Wilcoxon Signed–Rank Tests, Phi (φ) for chi-square analyses, partial eta squared (η^2_{partial}) for mixed ANOVA, and d for Bonferroni (Cohen, 1988; Tomczak & Tomczak, 2014). Cohen's descriptions for $\eta^2_{\text{(partial)}}$ (large effect: .14, medium effect: .06, small effect: .01), for r and φ (large effect: .5, medium effect: .3, small effect: .1), and for d (large effect: .8, medium effect: .5, small effect: .2) were used (Cohen, 1988).

4 RESULTS

4.1 PARTICIPANT CHARACTERISTICS

Table 3 (method section) lays out the demographic and clinical details of the participants. The participant groups did not display any significant differences in terms of age, gender, handedness, years of education, self-reported depressive symptoms, or alcohol consumption. In comparing the two patient groups, no significant differences were found in self-reported cognitive and emotional symptoms, lesion type, days postonset of stroke, or outpatient rehabilitation sessions prior to the study, or in types of outpatient rehabilitation. However, the RHS group showed significantly more visual neglect than the LHS group at an early stage of recovery, during ward care.

4.2 NEUROPSYCHOLOGICAL EXAMINATION

Details of the neuropsychological tests are listed in Table 4, and statistical analyses of the group differences are laid out in Table 6. Both of the patient groups exhibited significant differences compared to the controls in various tests assessing executive functions and processing speed, but significant differences were absent between the patient groups in analyses conducted for any of the utilized tests. LHS patients performed significantly worse than controls in phonetic fluency, RHS patients likewise fell short from controls in semantic fluency, and both patient groups also performed worse than controls in design fluency. LHS patients cancelled significantly fewer dot targets in the B-W single and dual tasks and counted significantly fewer numbers in the B-W dual task than controls did. In the TM A, the performance of RHS patients was significantly slower compared to the controls. Comparisons of performance in Letter-Number Sequencing (WMS-III) indicated significant group differences, but this finding was not supported by pairwise comparisons, where no such differences were detected.

4.3 LARGE-SCREEN DUAL TASKS IN REVEALING SUBTLE VISUAL NEGLECT (STUDY I)

4.3.1 OMISSIONS IN THE DETECTION AND THE CRASH DUAL TASKS

The average proportions of left-sided and right-sided omissions together with the relevant statistical analyses for the Detection and Crash Tasks are laid out in Table 7. One RHS patient was not able to perform the Crash Task, due to which the data of one patient is missing (indicated in Tables 7 and 8).

In the between-groups analyses, RHS patients exhibited significantly more omissions on the left side than controls did in both the Detection and Crash Tasks (see Figure 6). When comparing LHS patients with controls, no significant differences in the proportion of left-sided omissions were found, and the same remained true when comparing the two patient groups for both large-screen dual tasks. No significant group differences were found for omissions on the right side for the Detection or Crash Tasks.

Table 6 The performance of participant groups in the neuropsychological tests.

Neuropsychological variable[a]	LHS patients	RHS patients	Controls	Compared pairs	Statistics[b]	df	*P* value[c]	Effect size[d]
	N = 20	N = 20	N = 20					
VISUAL ATTENTION								
Bells Test								
left-sided omissions	1 (1)	1 (1)	1 (1)		3.011	2	.222	
right-sided omissions	1 (1)	1 (1)	0 (1)		4.973	2	.083	
EXECUTIVE FUNCTIONS AND PROCESSING SPEED								
Bells Test (s)[e]	126 (42)	145 (70)	124 (41)		1.009	2	.604	
TM A (s)	42 (20)	49 (23)	29 (9)		10.960	2	**.004**	η^2 = .157***
mean ranks	32.23	38.65	20.62					
				Controls vs. RHS	18.025		**.003**	*r* = .52***
				LHS vs. RHS	6.425		.733	
				Controls vs. LHS	11.600		.107	
TM B (s)	103 (62)	94 (36)	71 (26)		5.252	2	.072	
Brixton	14 (6)	16 (6)	12 (4)		4.884	2	.087	
Phonetic fluency	14 (6)	17 (4)	21 (7)		8.317	2	**.016**	η^2 = .111**
mean ranks	22.75	30.12	38.62					
				LHS vs. Controls	-15.875		**.012**	*r* = -.46**
				LHS vs. RHS	7.375		.542	
				RHS vs. Controls	-8.500		.369	
Semantic fluency	21 (8)	21 (5)	26 (6)		9.300	2	**.010**	η^2 = .128**
mean ranks	27.07	24.35	40.08					
				RHS vs. Controls	-15.725		**.013**	*r* = -.45**
				RHS vs. LHS	-2.725		1.000	
				LHS vs. Controls	-13.000		.055	
Design fluency	8 (3)	8 (3)	11 (4)		13.952	2	**.001**	η^2 = .210***
mean ranks	23.68	25.52	42.30					
				LHS vs. Controls	-18.625		**.002**	*r* = -.54***
				RHS vs. Controls	-16.775		**.007**	*r* = -.48**
				LHS vs. RHS	1.850		1.000	
B-W single task (numbers, amount)	43 (12)	42 (14)	49 (15)		1.991	2	.370	
B-W dual task (numbers, amount)	23 (8)	25 (9)	31 (11)		6.672	2	**.036**	η^2 = .082**
mean ranks	23.85	29.62	38.02					
				LHS vs. Controls	-14.175		**.031**	*r* = -.41**
				LHS vs. RHS	5.775		.886	
				RHS vs. Controls	-8.400		.384	
B-W single task (dots, amount)	28 (8)	28 (8)	34 (7)		7.638	2	**.022**	η^2 = .099**
mean ranks	25.88	26.32	39.30					
				LHS vs. Controls	-13.425		**.045**	*r* = -.38**
				LHS vs. RHS	.450		1.000	
				RHS vs. Controls	-12.975		.056	
B-W dual task (dots, amount)	18 (7)	20 (6)	25 (7)		9.424	2	**.009**	η^2 = .130**
mean ranks	23.02	28.77	39.70					
				LHS vs. Controls	-16.675		**.008**	*r* = -.38**
				LHS vs. RHS	5.750		.892	
				RHS vs. Controls	-10.925		.143	
MEMORY								
Visual Memory Span	15 (4)	14 (3)	16 (4)		4.084	2	.130	
Letter–Number Sequencing	9 (3)	9 (3)	11 (2)		6.434	2	**.040**	η^2 = .078**
mean ranks	27.45	25.60	38.45					
				RHS vs. Controls	-12.850		.057	
				RHS vs. LHS	-1.850		1.000	
				LHS vs. Controls	-11.000		.134	
Working memory distraction task	14 (4)	14 (3)	16 (2)		5.046	2	.080	
Word list learning task	28 (6)	32 (6)	32 (5)		5.082	2	.079	
Delayed recall of the wordlist	7 (2)	7 (3)	8 (2)		4.346	2	.114	

[a] Mean (standard deviation); [b] Kruskal–Wallis Test (χ^2); mean ranks, effect sizes, and *post hoc* comparisons given for significant group differences

[c] *P* values smaller than .05 are statistically significant (in bold); for pairwise comparisons *P*-value adjustments made with the Bonferroni correction

[d] Effect sizes according to Cohen (1988): η^2 = *small >.01, **medium >.06, ***large >.14, and *r* = *small >.1, **medium >.3, ***large >.5
LHS/RHS = left/right hemisphere stroke; B-W = Bourdon Wiersma; TM = Trail Making Test; df = degrees of freedom
Brixton = Brixton Spatial Anticipation Test; [e] Unpublished data; rest of the analyses presented in Study I

In the within-group analyses, RHS patients exhibited significantly more omissions for left-sided than right-sided Detection targets but no similar significant differences were observed in comparisons made between the two hemifields in LHS patients or controls. Controls exhibited significantly more omissions for Crash targets on the right side than the left side, but no significant differences between the hemifields were found within the LHS or RHS patients.

Table 7 Average left-sided and right-sided omissions in the Detection and Crash Tasks and related between-groups (top) and within-group (bottom) comparisons.

	LHS patients N = 20	RHS patients N = 20	Controls N = 20	Compared pairs	Statistics	df	*P* value[b]	Effect size[c]
Between-groups comparisons[a]								
Detection dual task	Average omissions (%)							
Left hemifield	8%	15%	3%		6.473	2	**.039**	η^2 = .078**
Mean ranks	30.40	36.90	24.20					
				Controls vs. RHS	-12.700		**.033**	*r* = -.40**
				LHS vs. RHS	6.500		.579	
				Controls vs. LHS	-6.200		.643	
Right hemifield	7%	4%	2%		2.355	2	.308	
Crash dual task	Average omissions (%)							
Left hemifield	15%	29%[e]	7%		8.404	2	**.015**	η^2 = .114**
Mean ranks	30.73	37.68	21.98					
				Controls vs. RHS	-15.709		**.012**	*r* = -.46**
				LHS vs. RHS	6.959		.602	
				Controls vs. LHS	-8.750		.309	
Right hemifield	20%	19%[e]	12%		3.289	2	.193	
Within-group comparisons[d]								
Detection dual task								
LHS patients				Right vs. Left	-.472		.637	
RHS patients				Right vs. Left	-2.234		**.025**	*r* = -.50***
Controls				Right vs. Left	-.447		.655	
Crash dual task								
LHS patients				Right vs. Left	-1.738		.082	
RHS patients				Right vs. Left	-1.386		.166	
Controls				Right vs. Left	-2.278		**.023**	*r* = -.51***

[a]Kruskal–Wallis Test (χ^2); mean ranks, effect sizes, and *post hoc* comparisons given for significant group differences

[b]*P* values smaller than .05 are statistically significant (in bold); for multiple pairwise comparisons *P* values adjusted with the Bonferroni correction

[c]Effect sizes according to Cohen (1988): η^2 = *small ≥.01, **medium ≥.06, ***large ≥.14, and *r* = *small ≥.1, **medium ≥.3, ***large ≥.5

[d]Wilcoxon Signed–Rank Test (Z); effect sizes given for significant differences

LHS = left-hemisphere stroke; RHS right-hemisphere stroke; df = degrees of freedom; Left/Right = Left/Right hemifield; [e]Data for one patient missing

4.3.2 REACTION TIMES IN THE DETECTION AND CRASH DUAL TASKS

Average RTs (with SDs) in the Detection and Crash Tasks, and the statistical analyses conducted thereon, are laid out in detail in Table 8. The participant groups did not exhibit significant differences from each other in their RTs to the targets of the Detection or Crash Tasks. However, in all groups, responses to the targets were significantly faster in the Detection Task than in the Crash Task (resulting in a significant *task* but not *task × group* effect). All groups also responded significantly faster to the right-sided rather than left-sided targets in the Crash Task (a significant *hemifield × task* but not *hemifield × task × group* effect).

Table 8 Average RTs in the Detection and Crash Tasks.

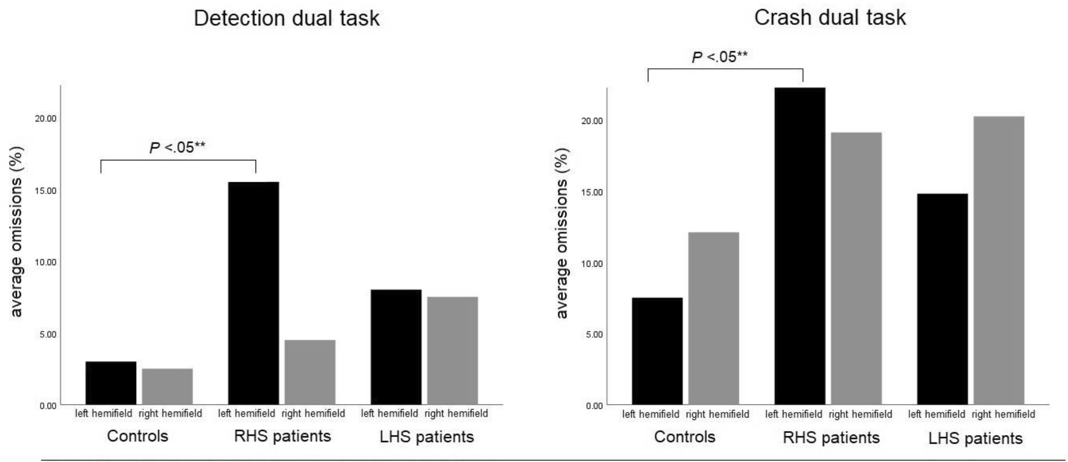
	Average RTs (SDs), ms		Statistics[a]	df	*P* value[b]	Effect size[c]
	Left hemifield	Right hemifield				
Detection dual task						
LHS patients N = 20	508 (60)	525 (62)				
RHS patients N = 20	534 (77)	533 (87)				
Controls N = 20	489 (55)	491 (52)				
Crash dual task						
LHS patients N = 20	721 (106)	704 (84)				
RHS patients N = 20	739 (89)[d]	708 (101)[d]				
Controls N = 20	670 (89)	657 (93)				
Between-participants effects			3.049	2	.055	
Within-participants effects		Hemifield	.960; 2.333	1	.132	
		Hemifield × Group	.966; 0.986	2	.379	
		Task	.141; 342.371	1	**< .001**	$\eta^2_{partial}$ = .859***
		Task × Group	.982; 0.501	2	.609	
		Hemifield × Task	.899; 6.272	1	**.015**	$\eta^2_{partial}$ = .101**
		Hemifield × Task × Group	.991; 0.246	2	.783	

[a] Mixed ANOVA (Wilks λ ; *F*)

[b] *P* values smaller than .05 are statistically significant (in bold); for multiple pairwise comparisons, *P*-value adjustments made with the Bonferroni correction; effect sizes given for significant effects

[c] Effect sizes according to Cohen, 1988: $\eta^2_{partial}$ = *small >.01, **medium >.06, ***large >.14; [d] Data for one patient missing

RT = reaction time; SD = standard deviation; LHS = left-hemisphere stroke; RHS = right-hemisphere stroke; df = degrees of freedom



RHS = right-hemisphere stroke; LHS = left-hemisphere stroke; N = 20 in all groups

Figure 6 Average proportions of omissions in the Detection (left panel) and Crash (right panel) dual tasks presented separately for each group and hemifield. Analyses for both large-screen dual tasks showed that RHS patients exhibited significantly more omissions for left-sided targets than the controls did (**medium effects).

4.4 COMPUTER METHODS IN REVEALING CONTRALESIONAL AND GENERAL DEFICITS IN VISUAL ATTENTION (STUDY II)

4.4.1 CONTRALESIONAL DEFICITS IN VISUAL ATTENTION: ASYMMETRY INDICES FOR THE BELLS TEST AND FOR THE LATERALIZED TARGETS COMPUTER TASK

Average AIs for the Bells Test and for the LTCT, as well as the related within-group analyses, are displayed in Table 9 (top). The expected value of the AI is zero, from which no group deviated significantly, either in the Bells Test or in the unilateral trials of the LTCT. However, RHS patients' AIs did differ significantly from zero, in bilateral trials. On average, RHS patients produced negative AIs, which indicate a predominance of left-sided omissions (see Figure 7). In the bilateral trials of the LTCT, AIs did not deviate significantly from zero within the LHS patient or control groups.

Table 9 Average AIs for the Bells Test and for the LTCT, and related within-group (top) and between-groups (bottom) comparisons.

	Average AIs^{b}	Statistics	*P* value^{c}	Effect size^{d}
Within-group comparisons^{a}				
Bells Test				
LHS patients N = 20	.15	1.359	.174	
RHS patients N = 20	-.25	0.942	.346	
Controls N = 20	-.45	1.425	.154	
LTCT				
Unilateral trials				
LHS patients N = 20	.15	0.905	.366	
RHS patients N = 20	-.40	-1.000	.317	
Controls N = 20	.10	0.816	.414	
Bilateral trials				
LHS patients N = 20	.55	1.119	.263	
RHS patients N = 20	-.70	-2.488	**.013**	*r* = -.56***
Controls N = 20	.00	0.000	1.000	

	Mean ranks^{e}	Compaired pairs	Statistics	df	Observed *P* values^{c,f}	Adjusted *P* values^{c,f}	Rank	Critical *P* values^{f}	Effect size^{d}
Between-groups comparisons^{e}									
Bells Test			3.625	2	.163				
LTCT									
Unilateral trials			1.683	2	.431				
Bilateral trials			9.032	2	**.011**				η^2 = .12**
LHS patients N = 20	35.02	RHS vs. LHS	-12.375		**.006**	**.018**	1	.017	*r* = -.43**
RHS patients N = 20	22.65	RHS vs. Controls	-11.175		**.014**	**.019**	2	.038	*r* = -.39**
Controls N = 20	33.83	Controls vs. LHS	1.200		1.000	NS	3	.150	

[a] Wilcoxon Signed–Rank Test (*Z*): deviation of the AI from zero; [b] AI represents spatial asymmetry in omission errors, negative values equal to dominance of left-sided omission errors, positive values dominance of right-sided omission errors, and zero indicates that omissions are distributed equally between the two hemifields

[c] *P* values smaller than .05 are statistically significant (marked in bold); effect sizes given for significant differences

[d] Effect sizes according to Cohen, 1988: *r* = *small >.1, **medium >.3, ***large >.5, and η^2 = *small >.01, **medium >.06, ***large >.14

[e] Kruskall–Wallis Test (χ^2); mean ranks and paired comparisons given for significant group differences

[f] A step-down multiple hypotheses testing procedure: adjusted and critical *P* values determined in order to control the family-wise error; observed *P* values that are smaller than the critical *P* values are statistically significant

LTCT = Lateralized Targets Computer Task; AI = Asymmetry index; NS = not significant; LHS = left-hemisphere stroke; RHS = right-hemisphere stroke

Rank = order of the compaired pairs (the smaller the *P* value the smaller the Rank); df = degrees of freedom

Statistical group comparisons of the AIs for the Bells Test and for the LTCT are displayed in Table 9 (bottom). The participant groups did not exhibit significant differences from each other in AIs for the Bells Test or the unilateral trials of the LTCT. However, in bilateral trials, RHS patients' AIs deviated significantly from those of the other two groups (see Figure 7).

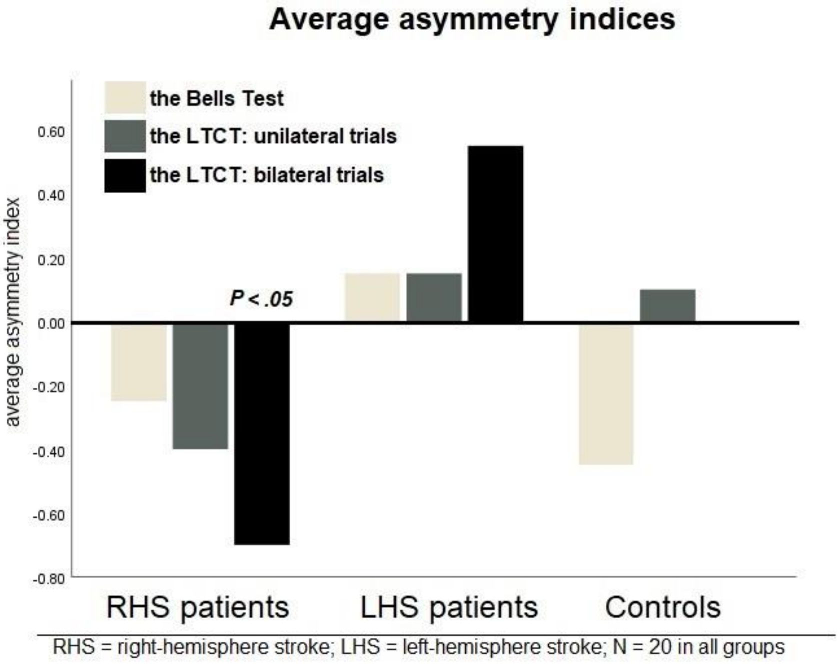


Figure 7 Average Asymmetry indices (AIs) in the Bells Test and LTCT for each group. In RHS patients, a significant deviation from the expected value of zero was found (*P* < .05; large effects), and from AIs of the other groups (*P* < .05; medium effects) in bilateral trials of the LTCT. The finding indicates a significant predominance of left-sided omissions in RHS patients.

4.4.2 GENERAL DEFICITS IN VISUAL ATTENTION: OMISSIONS AND REACTION TIMES IN THE BALL RAIN TASK

Average omissions for the Ball Rain Task, and the conducted within-group and between groups analyses, are displayed in Table 10. No significant differences between the omissions on the left side and the right side were observed within any of the participant groups (Table 10, top). However, group comparisons of left-sided and right-sided targets indicated that, for both sides, the LHS and the RHS patient groups missed significantly more targets than the control group did (Table 10, bottom; Figure 8).

Average RTs in the Ball Rain Task, together with the respective statistical analyses, are displayed in Table 11. The RTs were significantly slower for the targets of the Ball Rain Task for both patient groups than the controls. Same was found to be true for both hemifields because no *hemifield* or *hemifield × group* effects were found.

Table 10 Response omissions in the Ball Rain Task and related within-group (top) and between-groups (bottom) comparisons.

	Average omissions (%)	Statistics	P value
Within-group comparisons^{a}			
Ball Rain	Left vs. Right		
LHS patients N = 20	3% vs. 5%	-1.235	.217
RHS patients N = 20	5% vs. 4%	-.578	.563
Controls N = 20	1% vs. 1%	-.905	.366

	Mean ranks^{c}	Compaired pairs	Statistics	df	Observed P values^{b,d}	Adjusted P values^{b,d}	Rank	Critical P values^{d}	Effect size^{e}
Between-groups comparisons^{c}									
Ball Rain									
Left-sided omissions			10.093	2	**.006**				η^2 = .142***
LHS patients N = 20	32.73	Controls vs. RHS	-16.175		**.002**	**.006**	1	.017	r = -.489**
RHS patients N = 20	37.48	Controls vs. LHS	-11.425		**.029**	**.038**	2	.038	r = -.345**
Controls N = 20	21.30	RHS vs. LHS	4.750		.364	NS	3	.150	
Right-sided omissions			9.625	2	**.008**				η^2 = .134**
LHS patients N = 20	33.80	Controls vs. RHS	-15.450		**.004**	**.012**	1	.017	r = -.460**
RHS patients N = 20	36.58	Controls vs. LHS	-12.675		**.017**	**.022**	2	.038	r = -.377**
Controls N = 20	21.12	RHS vs. LHS	2.775		.601	NS	3	.150	

^{a}Wilcoxon Signed–Rank Test (Z); ^{b}P values smaller than .05 are statistically significant (in bold)

^{c}Kruskall–Wallis Test (χ^2); mean ranks, paired comparisons, and effect sizes given for significant group differences

^{d}A step-down multiple hypotheses testing procedure: adjusted and critical P values extracted to control the family-wise error, observed P values smaller than the critical P values are statistically significant

^{e}Effect sizes according to Cohen, 1988: η^2 = *small >.01, **medium >.06, ***large >.14, and r = *small >.1, **medium >.3, ***large >.5
NS = not significant; LHS = left-hemisphere stroke; RHS = right-hemisphere stroke
Rank = order of the compaired pairs (the smaller the P value the smaller the Rank); df = degrees of freedom

Table 11 Average RTs in the Ball Rain Task.

	Average RTs (SDs), ms			Statistics^{a}	df	P value^{b}	Effect size^{c}
	Left hemifield	Right hemifield					
Ball Rain Task							
LHS patients N = 20	532 (62)	551 (71)					
RHS patients N = 20	542 (74)	549 (84)					
Controls N = 20	480 (49)	476 (42)					
Between-participants effects				7.172	2	**.002**	$\eta^2_{partial}$ = .201***
Post hoc comparisons		95% confidence interval for difference					
	Mean difference	Lower bound	Upper bound				
Controls vs. RHS patients	-67.56 ms	-116.98 ms	-18.15 ms			**.004**	d = 1.04***
LHS patients vs. RHS patients	-3.89 ms	-53.31 ms	45.52 ms			1.000	
Controls vs. LHS patients	-63.67 ms	-113.09 ms	-14.26 ms			**.007**	d = 1.12***
Within-participants effects		Hemifield		.950; 2.986	1	.089	
		Hemifield × Group		.914; 2.696	2	.076	

^{a}Mixed ANOVA (Wilks λ ; F); *post hoc* comparisons and effect sizes given for significant group differences

^{b}P values smaller than .05 are statistically significant (marked in bold);
for multiple pairwise comparisons, P values adjusted with the Bonferroni correction

^{c}Effect sizes according to Cohen, 1988:
$\eta^2_{partial}$ = *small >.01, **medium >.06, ***large >.14, and d = *small >.2, **medium >.5, ***large >.8

RT = reaction time; SD = standard deviation; LHS = left-hemisphere stroke; RHS = right-hemisphere stroke; df = degrees of freedom

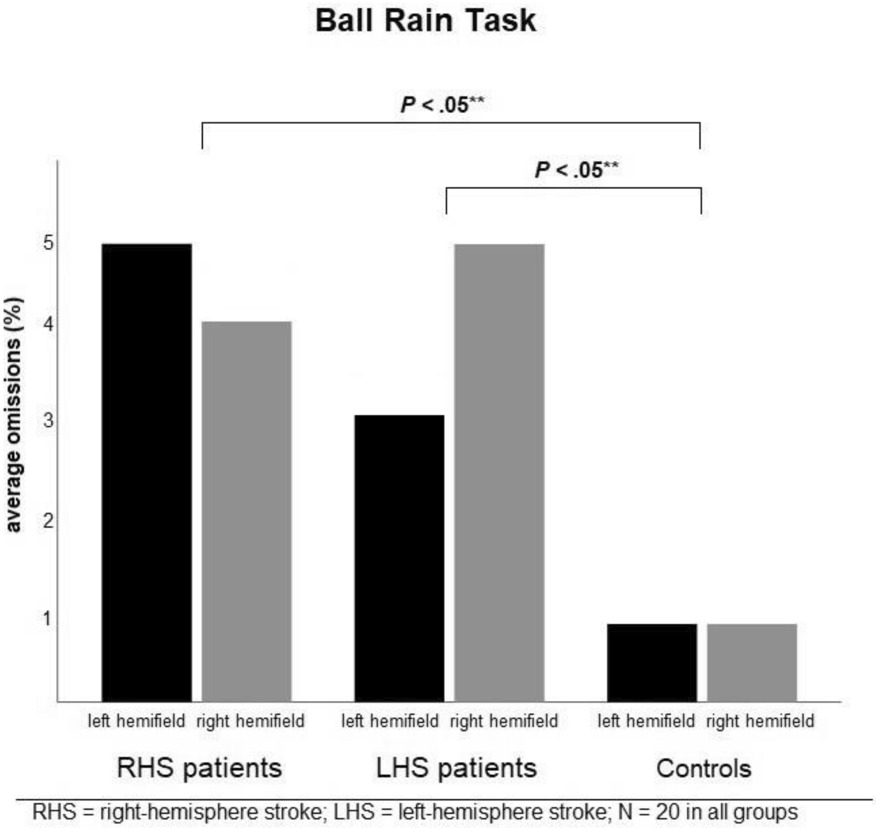


Figure 8 Average proportions of omissions in the Ball Rain Task presented for each group and hemifield. Patient groups missed significantly more targets than the control group in both of the two hemifields (**medium effects).

4.5 LARGE-SCREEN CANCELLATION TASK AND STANDARD-SCREEN DUAL TASKS IN DETECTING SPATIAL BIAS IN VISUAL ATTENTION (STUDY III)

4.5.1 OMISSIONS, MEAN POSITION OF HITS, STARTING POINTS, AND PERFORMANCE TIMES FOR THE TWINKLE CANCELLATION TASK

Omissions. Average proportion of omissions for the large-screen and PnP versions of the Twinkle Task, together with the statistical group comparisons performed thereon, are displayed in Table 12 (top). In the PnP version, no significant differences were observed between participant groups for omissions in either hemifield. However, in the large-screen version, LHS patients produced significantly more omissions for right-sided targets than controls. In terms of omissions exhibited on the right side, no significant differences were found in analyses conducted between the RHS patients and the controls, or between the RHS patients and the LHS patients. In the large-screen version, no significant group differences were found in terms of omissions exhibited on the left side. Table 12 (bottom) lays out the within-group comparisons for omissions on the left and right sides of the two Twinkle Task versions. None of the participant groups exhibited any significant differences between the two hemifields in the Twinkle Task, either in the large-screen or the PnP version.

Table 12 Between-groups (top) and within-group (bottom) comparisons for the large-screen and PnP versions of the Twinkle Task.

TWINKLE TASK	LHS patients N = 20	RHS patients N = 20	Controls N = 20	Compaired pairs	Statistics	df	*P* value^{b}	Effect size^{c}
Between-groups comparisons^{a}								
Large-screen version: average left-sided omissions	1%	1%	1%		.670	2	.715	
Large-screen version: average right-sided omissions	2%	2%	0%		6.190	2	**.045**	η^2 = .074**
mean ranks	35.62	31.02	24.85	Controls vs. RHS	6.175		.466	
				RHS vs. LHS	- 4.600		.870	
				Controls vs. LHS	10.775		**.040**	*r* = .392**
Large-screen version: average MPHs^{d}	-.00036	-.00067	-.00021		1.572	2	.456	
Large-screen version: average SPs^{e}	230	318	260		3.823	2	.148	
Large-screen version: average performance times, s (SD)	137 (32)	146 (29)	127 (28)		3.481	2	.175	
PnP version: average left-sided omissions	2%	2%	1%		1.714	2	.424	
PnP version: average right-sided omissions	1%	1%	1%		1.108	2	.575	
PnP version: average MPHs	.00144	.00096	.00110		0.148	2	.929	
PnP version: average performance times, s (SD)	113 (29)	135 (51)^{g}	95 (21)		10.206	2	**.006**	η^2 = .144***
mean ranks	31.68	38.03	20.70	Controls vs. RHS	17.326		**.005**	*r* = .498**
				LHS vs. RHS	6.351		.745	
				Controls vs. LHS	10.975		.130	
Within-group comparisons^{f}								
Large-screen version: left-sided vs. right-sided omissions								
LHS patients N = 20					-1.732		.083	
RHS patients N = 20					-.108		.914	
Controls N = 20					-.707		.480	
PnP version: left-sided vs. right-sided omissions								
LHS patients N = 20					-.209		.834	
RHS patients N = 20					-1.155		.248	
Controls N = 20					-1.134		.257	
Performance times: large-screen vs. PnP versions								
LHS patients N = 20					-2.688		**.007**	*r* = -.601***
RHS patients N = 20					-1.248		.212	
Controls N = 20					-3.397		**.001**	*r* = -.760***

[a] Kruskall–Wallis Test (χ^2), mean ranks, *post hoc* comparisons, and effect sizes given for significant group differences

[b] *P* values smaller than .05 are statistically significant (marked in bold); for multiple pairwise comparisons *P* values adjusted with the Bonferroni correction

[c] Effect sizes according to Cohen, 1988: η^2 = *small >.01, **medium >.06, ***large >.14, and *r* = *small >.1, **medium >.3, ***large >.5

[d] MPH = Mean Position of Hits; i.e., the standardized value of the mean horizontal location (x coordinate, in pixels) of correctly selected targets across the task sheet
The range of the MPH was set so that the left-side limit was -0.5 and the right-side limit +0.5

[e] SP = starting point; coded according to horizontal location (x coordinate, in pixels) of the first selected target
The parameters for the locations of the starting point (i.e., target locations) were set so that the left-side limit was 38 pixels and the right-side limit 1254 pixels

[f] Wilcoxon Signed–Rank Test (Z); effect sizes given for significant differences

[g] Data for one patient missing; LHS = left-hemisphere stroke; RHS = right-hemisphere stroke; df = degrees of freedom; SD = standard deviation

Mean Position of Hits and starting points. Average MPHs of the large-screen and PnP versions of the Twinkle Task, and the SPs recorded in the large-screen version are displayed in Table 12 (top). Statistical analyses (Table 12, top) revealed no significant differences in MPHs or the SPs between any of the groups for the Twinkle Tasks.

Performance times. Table 12 (top) displays the average performance times observed in both the large-screen and PnP versions of the Twinkle Task, together with statistical group comparisons conducted thereon. The participant groups did not exhibit significant differences in the large-screen version. However, in the PnP version, the controls were significantly faster than RHS patients (see Figure 9), but no significant differences were found between the controls and LHS patients, or between the patient groups. Table 12 (bottom) displays the within-group performance time comparisons of the two Twinkle Task versions. LHS patients and the controls both performed significantly faster in the PnP version than they did in the large-screen version. This was not true for RHS patients because no significant differences were observed between their performance times in the two Twinkle Task versions. The performance time of one of the RHS patients is missing for the PnP version (indicated in Table 12).

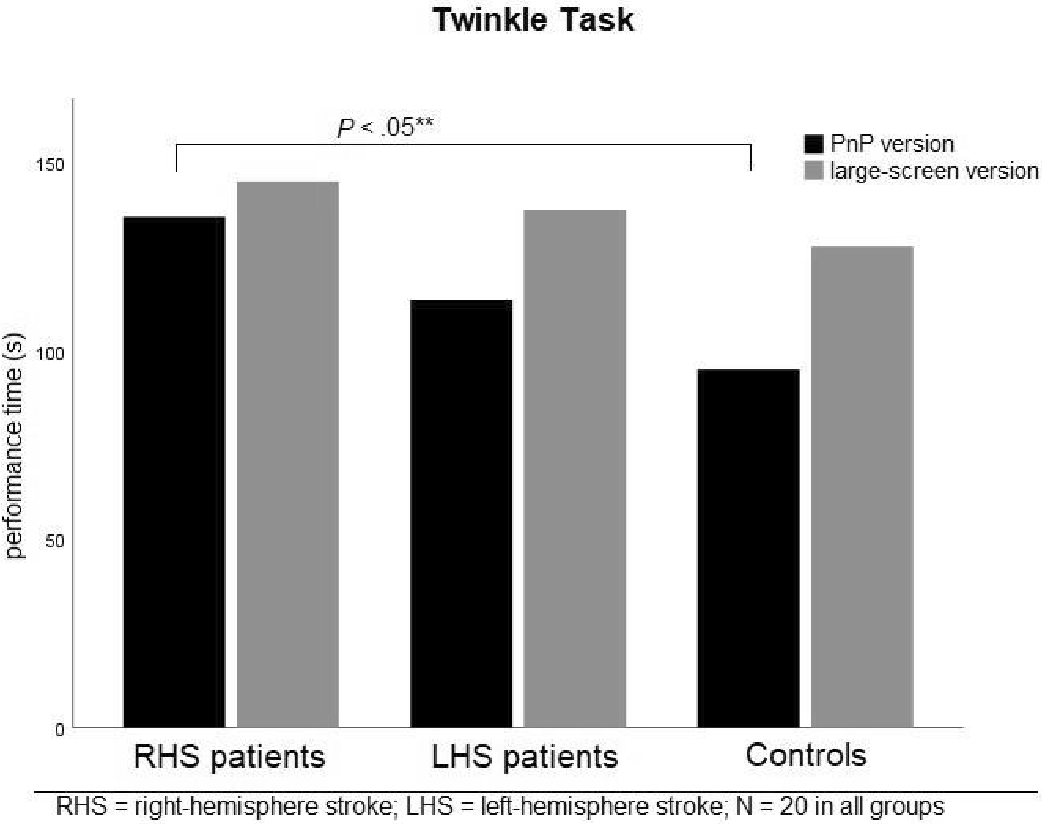


Figure 9 Performance times of the RHS and LHS patients, and controls, in the PnP and large-screen Twinkle Tasks. The controls were significantly faster than RHS patients in the PnP version (**medium effects).

4.5.2 OMISSIONS FOR UNILATERAL AND BILATERAL TRIALS OF THE VISUAL AND AUDITORY DUAL TASKS

Table 13 (top) lays out the average proportion of omissions observed in the Visual and Auditory dual tasks for both the unilateral and bilateral targets, together with the between-groups comparisons made thereon. RHS patients missed significantly more targets on the left side than controls did in both the unilateral and bilateral trials of the Visual dual task (see Figure 10). However, in comparisons between LHS patients and controls, as well as comparisons between LHS patient and RHS patient groups, no significant omission differences were observed in the Visual dual task. In the Auditory dual task, between-group comparisons yielded no significant differences in omissions in either the unilateral or bilateral trials. In the bilateral trials of the Auditory dual task, the main group comparison indicated a significant difference, but no supporting difference was observed in pairwise comparisons.

Table 13 Average omissions for the Visual and Auditory dual tasks, and related between-groups (top) and within-group (bottom) comparisons.

	LHS patients N = 20	RHS patients N = 20	Controls N = 20	Compaired pairs	Statistics	df	*P* value[b]	Effect size[c]
Between-groups comparisons[a]								
VISUAL AND AUDITORY DUAL TASKS: UNILATERAL TRIALS								
Visual dual task: left-sided omissions	4%	18%	2%		10.729	2	**.005**	$\eta^2 = .153$***
mean ranks	30.73	38.65	22.12	Controls vs. RHS	16.525		**.003**	*r* = .518***
				LHS vs. RHS	7.925		.349	
				Controls vs. LHS	8.600		.265	
Visual dual task: right-sided omissions	4%	12%	3%		3.715	2	.156	
Auditory dual task: left-sided omissions	3%	6%	2%		4.040	2	.133	
Auditory dual task: right-sided omissions	5%	6%	2%		1.617	2	.445	
VISUAL AND AUDITORY DUAL TASKS: BILATERAL TRIALS								
Visual dual task: left-sided omissions	1%	12%	1%		8.253	2	**.016**	$\eta^2 = .110$**
mean ranks	28.75	36.70	26.05	Controls vs. RHS	10.650		**.017**	*r* = .437**
				LHS vs. RHS	7.950		.117	
				Controls vs. LHS	2.700		1.000	
Visual dual task: right-sided omissions	6%	1%	1%		3.296	2	.192	
Auditory dual task: left-sided omissions	2%	7%	1%		6.033	2	**.049**	$\eta^2 = .071$**
mean ranks	27.68	36.30	27.52	Controls vs. RHS	8.775		.096	
				LHS vs. RHS	8.625		.105	
				Controls vs. LHS	0.150		1.000	
Auditory dual task: right-sided omissions	4%	1%	0%		0.477	2	.788	
Within-group comparisons[d]								
Visual dual task: left-sided vs. right-sided omissions								
unilateral trials								
LHS patients N = 20					-1.207		.227	
RHS patients N = 20					-1.712		.087	
Controls N = 20					-1.265		.206	
bilateral trials								
LHS patients N = 20					-1.403		.161	
RHS patients N = 20					-1.921		.055	
Controls N = 20					-0.557		.577	
Auditory dual task: left-sided vs. right-sided omissions								
unilateral trials								
LHS patients N = 20					-.586		.558	
RHS patients N = 20					-.359		.719	
Controls N = 20					-0.587		.557	
bilateral trials								
LHS patients N = 20					0.000		1.000	
RHS patients N = 20					-2.503		**.012**	*r* = -.560***
Controls N = 20					-1.134		.257	

[a] Kruskall–Wallis Test (χ^2), mean ranks, *post hoc* comparisons, and effect sizes presented for significant group differences

[b] *P* values smaller than .05 are statistically significant (in bold); for multiple pairwise comparisons *P* values adjusted with the Bonferroni correction

[c] Effect sizes according to Cohen, 1988: η^2 = *small >.01, **medium >.06, ***large >.14, and *r* = *small >.1, **medium >.3, ***large >.5

[d] Wilcoxon Signed–Rank Test (Z); effect sizes presented for significant differences

LHS = left-hemisphere stroke, RHS = right-hemisphere stroke; df = degrees of freedom

Table 13 (bottom) includes the details of the within-group comparisons for omissions between the left and the right side in the Visual and Auditory dual tasks. No significant differences were found for any of the groups in comparisons between omissions on the left and right side in the Visual dual task, or in the unilateral trials of the Auditory dual task. However, it was found that RHS patients missed significantly more targets on the left side than on the right side in bilateral trials of the Auditory dual task. Comparisons between hemifields did not show any significant differences in performance in the bilateral trials of the Auditory dual task for either LHS patients or controls.

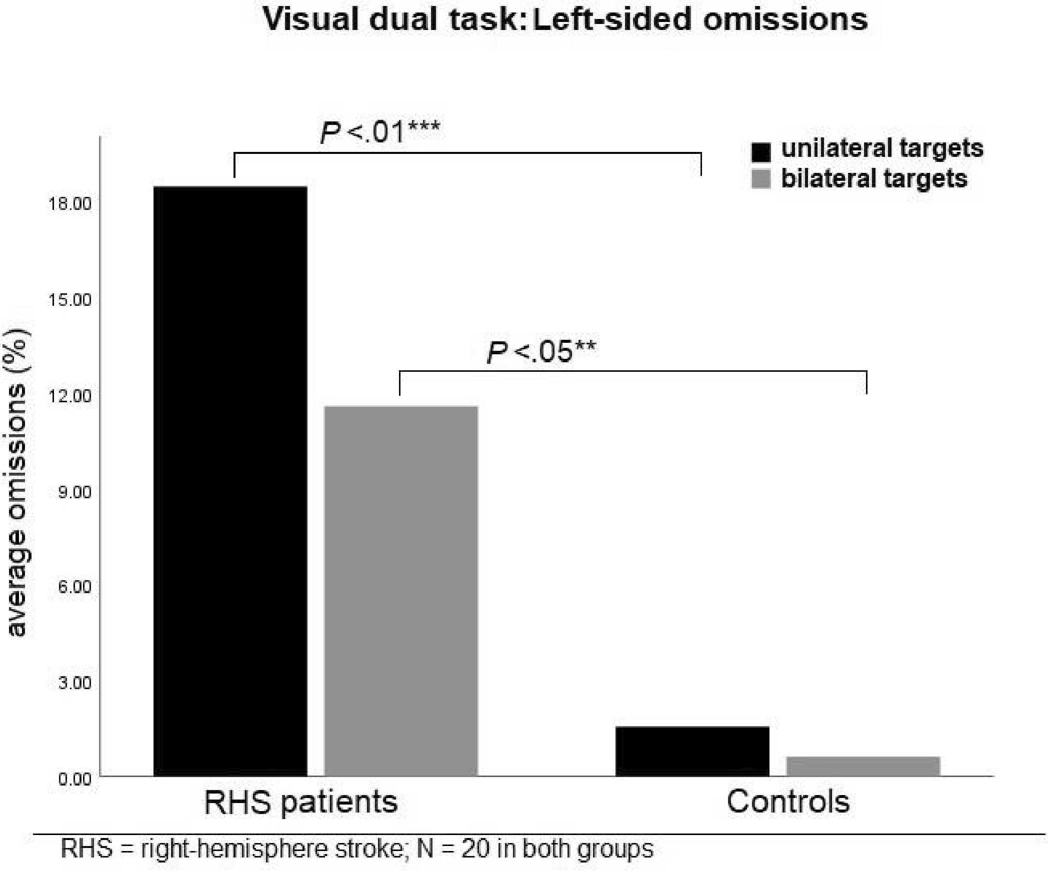


Figure 10 Average proportion of left-sided omissions of RHS patients and controls for the unilateral and bilateral targets of the Visual dual task. RHS patients missed significantly more left-sided unilateral (***large effect) and bilateral (**medium effect) targets than controls did.

5 DISCUSSION

Studies I–III of the present dissertation aimed to examine whether various aspects of visuoattentive deficits of unilateral stroke patients could sensitively be revealed with computer methods. A novel large-screen computer method was utilized together with another computer test battery, in order to answer each respective study question by comparing methods with different characteristics. The main findings were that RHS patients exhibited significant contralesional omissions for unilateral targets in the large-screen and standard-screen dual tasks, and for bilateral targets in the LTCT and in the standard-screen dual task. Moreover, LHS and RHS patient groups both showed significant omissions for targets in the large-screen Ball Rain Task contralesionally as well as ipsilesionally. These deficits were not observed with traditional cancellation-task approaches, despite attempts to increase the sensitivity by several means known for their effectiveness. The present findings indicate that patients with chronic unilateral stroke may show subtle visuoattentive deficits, which are not reliably detected with traditional cancellation tests. These deficits may be dependent on the location of the lesion. Different kinds of computer methods are needed to uncover subtle visuoattentive deficits.

5.1 COMPUTER DUAL TASKS IN REVEALING SUBTLE VISUAL NEGLECT AND EXTINCTION

The demographic and clinical characteristics of the participant groups were comparable in all features assessed, except in one—the prevalence of visual neglect at the early stage of recovery (13 days poststroke, on average). At that time, RHS patients exhibited significantly more neglect than LHS patients, according to the clinical neuropsychological assessments (Table 3). However, at the time that the study was conducted (106 days poststroke, on average), none of the RHS or LHS patients met the conventional criteria for neglect according to the Bells Test (see Section 3.5.2).

A dual-task setting was utilized in Studies I and III, to find out whether increasing the complexity and attentional demands of the tasks would uncover subtle neglect or extinction in the patient sample. Two different dual tasks with varying complexity were utilized and run on a large screen (Study I), and further, two standard-screen dual tasks with different secondary tasks were used (i.e., visual or auditory; Study III). All applied dual tasks showed significant contralesional omissions in RHS patients. These findings were in contradiction with the results of the Bells Test, but in line with several previous studies comparing computer and PnP tests (Deouell et al., 2005; Kim et al., 2010; Ulm et al., 2013; van Kessel et al., 2010; van Kessel et al., 2013). Taken together, the present and previous findings indicate that complex, attentionally demanding test environments are useful in revealing neglect-related symptoms, which are mild and are not detected with traditional methods (Blini et al., 2016; Bonato et al., 2010; Deouell et al., 2005; Hasegawa et al., 2011). Even these subclinical symptoms are important to diagnose because they may cause significant real-life problems (Bonato et al., 2012; Deouell et al., 2005; Jehkonen et al., 2000; Sotokawa et al., 2015).

Visual dual-task settings, in which brief lateralized targets are presented together with a secondary central task, seem to be particularly sensitive in inducing contralesional omissions (Andres et al., 2019; Bonato, 2015; Bonato et al., 2010, 2012). This might be attributable to the task demands hindering the use of coping mechanisms to compensate for neglect and extinction. Simultaneous processing of central and peripheral visual fields in a short timeframe is challenging and may leave neglect patients unable to compensate for underlying deficits (Andres et al., 2019; Bonato & Deouell, 2013; Russell et al., 2004). Types of demands in the secondary task other than visuoattentive ones also increase assessment sensitivity (Bonato et al., 2010; Mennemeier et al., 2004; Ricci et al., 2016; Robertson & Frasca, 1992). In Studies I and III, arithmetic processing was needed in the secondary tasks. This may have contributed in uncovering RHS patients' subtle neglect and extinction. It has been suggested (Ricci et al., 2016) that combining visuospatial and arithmetic processing induces both general and lateralized inattention which, when found together, exacerbates neglect symptoms (Husain & Rorden, 2003).

In the large-screen dual tasks, which were fast-paced in nature, sufficient processing speed and executive functions were needed in addition to visuoattentive and spatial functions. Effective working memory was required as well, at least in the central task of Crash. These same cognitive functions were largely affected in the patient sample (see Table 6), which is typical in stroke (Farnè et al., 2004; Jaillard et al., 2009; Jokinen et al., 2015; Middleton et al., 2014; Nys et al., 2005). Therefore, it may be that, due to these additional deficits, the patients had to work particularly hard when performing the large-screen dual tasks, and this further burdened their attentional resources and capacity to compensate for neglect (Smit et al., 2004a; van Kessel et al., 2010).

RT analyses of the large-screen dual tasks revealed that in all groups, responses to the targets of the simpler dual task (Detection) were significantly faster than those for the more complex dual task (Crash). This finding was quite expected (Bartolomeo, 2000). Surprisingly, however, the increment in task complexity did not induce neglect-related spatial bias in RTs, but rather triggered a general rightward shift. In all groups, responses to the right-sided targets of the Crash Task were significantly faster than those to the left-sided targets. Compared with the Detection Task, the Crash Task was more complex, twice as long in duration, and was performed last. It is possible that these factors decreased the participants' alertness due to depleted resources (Peers et al., 2006; Smit et al., 2004a, 2004b). Several studies have linked decreased (tonic) alertness to a rightward shift observed in patients suffering from right-hemisphere strokes (Peers et al., 2006; Robertson et al., 1997a), but also in patients with left-hemisphere strokes (Peers et al., 2006), and even healthy participants (Bellgrove et al., 2004; Dobler et al., 2005; Dodds et al., 2008; Fimm et al., 2006; Manly et al., 2005; Pérez et al., 2009; Takio et al., 2011, 2013). According to Bellgrove et al. (2004), the phenomenon could be explained by weakened ability to sustain attention being linked to weakened activity in frontoparietal attentional networks, which underlie sustained attention as well as spatial attention. Because the right hemisphere dominates both of these aspects of attention, and they are highly interconnected (Cavézian et al., 2015; Corbetta et al., 2005; He et al., 2007; Posner & Petersen, 1990; Robertson, 1989, 1993, 2001), a decrease in alertness and in activity of the attentional networks might weaken the right hemisphere's spatial attentional systems and drive attention rightward (see Bellgrove et al., 2004). Peers et al. (2006) proposed an alternative hypothesis after observing a general rightward shift under dual-task conditions in patients with stroke either on the right or the left hemisphere, and in healthy participants. According to Peers et al. (2006), dividing attention in a dual task may produce a similar functional effect as if alertness were decreased (without decreasing alertness itself). However, the present findings are not in line with this hypothesis because Detection was also a visual dual task but did not induce similar effect. This would suggest that the rightward shift observed in Crash may indeed be related to decreased alertness, attributable mainly to the depletion of resources caused by performing sustained and highly demanding tasks after having already completed several other tasks (Peers et al., 2006; Smit et al., 2004a, 2004b; Takio et al., 2014).

To conclude, a dual-task setting in which brief lateralized targets are presented together with a secondary task seems to be a very sensitive approach in detecting symptoms related to neglect in patients suffering from right-hemisphere stroke. This phenomenon seems to be independent of whether a dual task is fast-paced or not, and of the size of the test field.

5.2 CANCELLATION TASKS IN ASSESSING SUBTLE VISUAL NEGLECT

In Studies I and II, the visuoattentive functions of the participant groups were assessed with a traditional cancellation task, the Bells Test. First in Study I, total amount of left-sided and right-sided omissions was analyzed. Then in Study II, to gain further confirmation, relative proportion of left-sided vs. right-sided omissions (AIs) was scrutinized. Although RHS patients exhibited subtle neglect in large-screen dual tasks, no significant contralesional omissions were revealed in raw omission analyses or in AI analyses of the Bells Test (Tables 6 and 9). Therefore, additional analyses were introduced in Study III for the novel Twinkle cancellation task. Other factors known to increase sensitivity of neglect assessment were also used: high density of targets and their similarity with distractors (Aglioti et al., 1997; Basagni et al., 2017; Bickerton et al., 2011; Chatterjee et al., 1999; Rapcsak et al., 1989; Sarri et al., 2009; Ten Brink et al., 2020), and a time limit to prevent compensation in the large-screen version (Priftis et al., 2019). These manipulations were used as in previous studies similar factors have increased the sensitivity of PnP cancellation tasks (Basagni et al., 2017; Bickerton et al., 2011; Priftis et al., 2019; Sarri et al., 2009). Tasks analogous to PnP Twinkle Task have turned out to be more sensitive than the Bells Test (Basagni et al., 2017). However, even with these additional factors, Twinkle Task did not prove to be sensitive in uncovering contralesional omissions in RHS patients, either in the PnP format or the large-screen version (which supports the findings of Bonato et al., 2012). The starting-point analyses also failed to provide any further advantage in revealing RHS patients' subtle neglect (not in line with Azouvi et al., 2002; Nurmi et al., 2010; Nurmi et al., 2018; Priftis et al., 2019).

In the cancellation tasks, the only variable that differentiated RHS patients from the controls was performance time. The controls performed significantly faster than RHS patients in the PnP format iteration of the Twinkle Task. Unlike RHS patients, whose performance was consistently slow, both the controls and LHS patients exhibited a clear difference in performance between the two versions of the Twinkle Task. That is, they were significantly faster in the (not time-limited) PnP version as compared to the (time-limited) large-screen format. The large-screen version may have been more demanding to perform than the PnP version, which may explain this result. Slow processing observed in RHS patients may be a remnant of neglect (Bartolomeo & Chokron, 1999; Buxbaum et al., 2004; Nurmi et al., 2018; Samuelsson et al., 1998; Viken et al., 2014), although in the present study, the finding was not specifically limited to RHS patients, as it was also evident in LHS patients in other variables (Tables 6 and 11; Studies I and II).

LHS patients exhibited significantly worse performance than controls did in terms of the proportion of right-sided omissions in the large-screen Twinkle Task. It is plausible that the task was sensitive in uncovering LHS patients' neglect, as an attempt was made to increase task sensitivity by several means. The similarity of the targets and distractors in the Twinkle Task may have resulted in the task being more demanding from a visuoperceptual perspective, and this is reportedly a factor in achieving increased sensitivity in assessing neglect (Aglioti et al., 1997; Basagni et al., 2017; Riddoch & Humphreys, 1987). However, the fact that an equal number of omissions was observed in LHS and RHS patients, but only the difference between LHS patients and controls was statistically significant in pairwise comparisons (Table 12), might suggest that this is a chance finding. Further support for this interpretation comes from the absence of any sign of neglect in the results for LHS patients in either of the computer dual tasks, each of which uncovered significant contralesional omissions in RHS patients. It is also important to note that these same standard-screen dual tasks are evidently sensitive in detecting even subtle neglect in chronic left-hemisphere stroke patients (Blini et al., 2016; Bonato et al., 2010).

To conclude, the present findings indicate that cancellation tasks on their own are insufficient to accurately detect subtle neglect in patients with chronic right-hemisphere stroke, and instead, approaches that are more demanding from an attentional standpoint are required in clinical settings as diagnostic tools (Gammeri et al., 2020; Pedroli et al., 2015; Taylor, 2003). Learning can be one influencing factor, as cancellation tasks are commonly used in clinical evaluations, and also frequently in rehabilitation. It is likely that, with repeated exposure to a task, the test type becomes increasingly familiar and patients perform better as they learn to compensate for neglect (Danckert & Ferber, 2006; Erez et al., 2009; Ogourtsova et al., 2017; Parton et al., 2004; Schendel & Robertson, 2002; Spreij et al., 2020). In fact, Hasegawa and colleagues (2011) assessed the eye movements of a chronic-phase neglect patient and found that the patient had learned to compensate for (left) neglect in cancellation tasks. When the patient's performance was then assessed in daily living settings and activities, the tendency for rightward spatial bias became evident. Similar results on the ability of patients to compensate for neglect in visual searching have also been found, even if the test field is large (Nakatani et al., 2013). Other studies (Bonato et al., 2012; Deouell et al., 2005), on the other hand, have demonstrated that chronic neglect, which becomes evident in real-life situations but not through traditional tests, can be seen in attentionally demanding computer tasks. Therefore, in the chronic phase, dynamic and complex test environments with sufficient attentional demands are useful (Bonato & Deouell, 2013).

5.3 COMPUTER METHODS IN REVEALING CONTRALESIONAL AND GENERAL DEFICITS IN VISUAL ATTENTION

In Study II**,** two computer methods with different characteristics were compared to find out whether general (i.e., nonlateralized) visuoattentive deficits as well as contralesional deficits in visual attention could be observed in patients with left- or right-hemisphere stroke. To assess whether the patients exhibited general deficits, the Ball Rain Task was developed. The Ball Rain Task was designed to incorporate two qualities—visual stimuli, which are in motion, combined with a setting, which constantly requires fast-paced selective attention. These qualities have been identified in previous studies as being conducive to increased sensitivity in revealing visuoattentive deficits as nonlateralized (Battelli et al., 2001; Chokron et al., 2019; Rapcsak et al., 1989). In the assessment of contralesional deficits, the LTCT, the sensitivity of which has already been shown, was used (Bonato et al., 2012).

The main findings were that in the Ball Rain Task both LHS and RHS patients produced significantly more omissions and slower responses than controls did, with the same being true for the left as well as the right side (Tables 10 and 11). In the LTCT, the performance of RHS patients was not symmetrical in bilateral trials, as they exhibited significantly more omissions on the left side than on the right side (Table 9). LHS patients and controls did not exhibit spatial bias, which resulted in a significant difference between the RHS group and the other two groups on the distribution of omissions in bilateral trials (Table 9). Significant deficits in visual attention were not found in PnP tests (Tables 6, 9, and 12; Studies I–III). Apparently, moving stimuli that require fast-paced selective attention sensitively uncover general inattention, whereas briefly presented lateral targets are a better tool for measuring contralesional deficits.

The fact that both LHS and RHS patients exhibited bilateral deficits in the Ball Rain Task may be related to slow or inefficient processing. LHS patients showed slow processing in several neuropsychological tests (Table 6). Regarding RHS patients, this finding may be due to deficits in directing attention—in both time and space (Husain et al., 1997). It has been demonstrated that neglect patients need a significantly prolonged time between two targets to be able to report both reliably (Husain et al., 1997). The requirement of processing the movement of stimuli presumably uncovers this nonlateralized inability to allocate attention over time (Battelli et al., 2001; Husain et al., 1997). These kinds of deficits might explain the patients' difficulties with the Ball Rain Task: The attention given to one fast-moving stimulus was possibly made unavailable to other stimuli (Desimone & Duncan, 1995; Duncan et al., 1999), leading to the participants missing targets on a wide range.

The aforementioned results are congruent with previous studies (Battelli et al., 2001; Husain et al., 1997; Robertson et al., 1997a), indicating that patients suffering from right-hemisphere stroke may exhibit both contralesional deficits as well as nonlateralized deficits in visual attention. Importantly, the present findings expand on previous research (Chokron et al., 2019; Husain et al., 1997; Robertson et al., 1997a; Robertson et al., 1998) by showing that these deficits may also be detectable in patients whose symptoms are only subtle and are not evident with PnP methods. The fact that the Ball Rain Task specifically uncovered general inattention, whereas the LTCT (and the dual tasks; Tables 7,13) uncovered lateralized inattention, stresses the importance of using sensitive methods with differing qualities to detect various aspects of visuoattentive deficits. There are several reasons justifying the importance of diagnosing both general and lateralized inattention, and their possible co-occurrence. First, deficits in general attention constitute a significant marker of neglect (Robertson et al., 1997a), and they may intensify and lengthen the syndrome (Hjaltason et al., 1996; Husain & Rorden, 2003; Robertson, 2001; Samuelsson et al., 1998). Second, general inattention may be a remnant of neglect (Nurmi et al., 2018). Third, alleviating the general deficits may ameliorate the contralesional deficits (Robertson et al., 1995).

Which factors contributed to the Ball Rain Task revealing RHS patients' visuoattentive deficits as nonlateralized, whereas only contralesional deficits were seen in other tasks? It is possible that stimulus motion had an effect. Motion attracts attention (Wolfe & Horowitz, 2004), and attention is needed in perceiving motion (Beer & Röder, 2004; Cavanagh, 1992). The fact that attention is oriented toward motion (Hopfner et al., 2015) has led to a clinical finding of contralesional moving cues alleviating neglect (Butter & Kirsch, 1995; Butter et al., 1990; Hopfner et al., 2015). It is therefore possible that in the Ball Rain Task, the motion of the stimuli captured RHS patients' attention equally within both sides of the visual field. Nevertheless, it can be presumed that the patients exhibited more omissions than controls did across the visual field, mainly due to their underlying core attentional deficits and inefficient processing.

Yet another hypothesis concerning RHS patients leans on findings of attention being rightward biased in neglect (Butler et al., 2009; Gainotti et al., 1991; Mark et al., 1988). According to Snow and Mattingley (2006), this bias or "hyperattention" toward the right may lead to difficulty in efficiently inhibiting irrelevant information in the patients' right hemifield (see also Bays et al., 2010; Duncan et al., 1997; Shomstein et al., 2010). It is therefore possible that the deficits exhibited by RHS patients in the Ball Rain Task originated differently and through different mechanisms in the two hemifields. This hypothesis posits that the left-field deficit was related to dysfunction in spatial attention, whereas the right-field deficit was due to difficulty in filtering and processing visual information efficiently.

The present findings appear to support the concept that the right hemisphere plays a critical part in both spatially lateralized and nonlateralized attentional components and their interconnection (Bellgrove et al., 2004; Cavézian et al., 2015; Corbetta et al., 2000; Corbetta et al., 2005; Posner & Petersen, 1990; Robertson, 1989, 1993, 2001; Sturm & Willmes, 2001). It has been proposed that two attentional networks—the dorsal frontoparietal and the ventral—are involved in stimulus processing (Chang et al., 2013; Corbetta & Shulman, 2002; Corbetta et al., 2008). In particular, the ventral network is lateralized to the right hemisphere (Corbetta & Shulman, 2011). Apparently, the dorsal network is crucial in spatial attention, and the ventral network in nonspatial (i.e., general) attentional functions (Corbetta & Shulman, 2002; He et al., 2007). Although these networks are focused on different components of attention, effective attentional control is based on their close interaction (Vossel et al., 2014). Supporting evidence comes from brain imaging studies: Ventral lesions in the right hemisphere commonly cause neglect, but the core symptom is in spatial attention controlled by the dorsal regions (Corbetta & Shulman, 2011). Based on neuroimaging and behavioral findings, Corbetta and Shulman (2011) propose that right ventral lesions impair nonspatial attentional functions controlled by the ventral network and induce physiological abnormalities in the dorsal network, which controls spatial attention. Hence, as suggested by He and colleagues (2007) and Chokron and colleagues (2019), neglect presumably occurs due to the interaction between structural and functional damage to both of these networks (see also Corbetta et al., 2005). This might explain the fact that neglect patients also show general attention deficits (Chokron et al., 2019).

5.4 STRENGTHS AND LIMITATIONS

From a methodological viewpoint, the comprehensive battery of largely novel computer tests aimed at identifying any deficits in visual attention can be regarded as a marked strength of the present study. To my knowledge, the present studies are one of the first to compare several distinct computer methods in an effort to map their ability to identify different aspects of visual inattention and improve the assessment of mild deficits.

Despite its advantages, the present study also has some limitations to consider when interpreting the results. First, a clear limitation on the general applicability of the findings is set by the limited sample size. A “clean” sample of stroke patients was attempted to gain by excluding patients with bilateral or previously diagnosed stroke, patients with other neurological diagnoses affecting cognition, and patients with visual field deficits. There were also several other inclusion and exclusion criteria (see Section 3.1). Given these criteria, it was not possible to recruit more patients without significantly prolonging the study. However, this is not atypical, but rather the norm. Studies assessing novel methods to reveal brain-damaged patients’ visuoattentive deficits frequently use small sample sizes (see e.g., Andres et al., 2019; Bonato et al., 2010; Kim et al., 2010; Ota et al., 2001; Priftis et al., 2019; Ulm et al., 2013; van Kessel et al., 2010, 2013). Various factors are surely at play here, but the piloting process necessary in the development of new methods, meaning a need to receive initial data to support further improvement on a relatively tight research schedule, is certainly a key factor. Therefore, if necessary, as is frequently the case, such initial pilot studies are conducted utilizing a slightly smaller sample size. Nevertheless, small sample size combined with the fact that these are the first-ever results with the new methods clearly require additional research to verify the present results and to enable generalizations to be made.

The patient participants were selected based on neuropsychological symptoms and the related clinically assessed need for rehabilitation. The neurological data was based on information collected in clinical practice, therefore, stroke scales (e.g., National Institutes of Health Stroke Scales, NIHSS; Brott et al., 1989, and modified Ranking Scale, mRS; van Swieten et al., 1988) or scales assessing everyday behavior (e.g., Barthel Index; Mahoney & Barthel, 1965, and Functional Independence Measure, FIM; Granger et al., 1993) were not systematically carried out. Catherine Bergego Scale (Azouvi et al., 1996; Bergego et al., 1995) that assesses neglect in real-life situations was not used either. However, lacking information seems to not be crucial in the present study because 1) the Barthel Index, FIM, and Catherine Bergego Scale only measure basic functions (e.g., eating, dressing), so they appear to be inaccurate in detecting subtle neglect in everyday activities (Bonato, 2012); and 2) mRS and NIHSS appear to be insensitive in detecting stroke-related cognitive symptoms (Jokinen et al., 2015; Kauranen et al., 2014), and especially neglect (Gottesman & Hillis, 2010; Hillis et al., 2003). For the same aforementioned reason, no specific lesion volume or lesion location analysis was made, as the patients were classified into their respective subgroups (LHS/RHS) based on clinical neurological and imaging findings. The additional information would have provided valuable insights regarding the interconnection of visuoattentive deficits and the clinical details of the present stroke patients. However, the focus of this initial-phase study was in the development of the new methods and their neuropsychological piloting.

The control group was matched with the patients for demographic characteristics, and no significant differences were observed either between the patient groups. However, one trend-level difference was found as 55% of the participants in RHS group but only 25% in LHS group were female (*P* = .056). Some studies have reported that there are no differences between genders in the incidence of visuoattentive deficits after unilateral stroke (McGlone et al., 1997). Other studies, however, have found that neglect is more frequent in women (Hammerbeck et al., 2019). As there were slightly more women in the RHS group than in the LHS group, the gender may have affected the results. In any case, additional studies are needed, as the observation was only a trend and the sample size was small.

Whereas in clinical practice a combination of PnP tests is typically used to diagnose visual neglect (e.g., BIT by Wilson et al., 1987), the only PnP methods employed in the present study were cancellation tasks. Neglect is a heterogeneous disorder, and PnP test findings may double-dissociate (Maeshima et al., 2001; Sacher et al., 2004). Therefore, the present study offers only some support to a conclusion that the computer methods used are more sensitive than PnP methods in general. However, there is evidence demonstrating that if unilateral stroke patients do not exhibit symptoms of neglect when undertaking tasks with the unilateral targets of the LTCT (as was the case in the present study), then they would not show neglect in various PnP tests that could have been included (e.g., BIT) (Blini et al., 2016; Bonato, 2015; Bonato et al., 2010). There is further evidence demonstrating in a group of right-hemisphere stroke patients that unilateral targets of the LTCT are more sensitive in identifying neglect than BIT (Bonato et al., 2012; Bonato et al., 2013). The present findings strongly suggest that the patient sample was not suffering from moderate or severe neglect, which BIT reliably and validly reveals (Halligan et al., 1991; Hannaford et al., 2003). Therefore, it is plausible that assessing visual neglect with more varied PnP methods would lead to similar results. The decision not to use additional PnP tests in the neglect assessment was due to the fact that the present participants already underwent an extensive test battery covering several computer methods, as well as PnP tests assessing various parts of cognition. Because of the already heavy load imposed by these tests, it was not possible to expand the test batteries in light of, for example, fatigue due to stroke.

The Bonferroni correction was used in statistical analyses to control for family-wise error, in all *post hoc* comparisons except in omission and AI analyses of Study II. The decision to replace the Bonferroni correction with a less conservative step-down multiple-hypotheses testing procedure was due to the fact that in the Ball Rain Task, the patient groups showed very similar omission rates, but only the difference between RHS patients and controls reached statistical significance with the Bonferroni correction. As first-ever results with new methods are presented here, it was considered important to also highlight the observation regarding LHS patients, which reached statistical significance with a less conservative method. The lack of significance with the Bonferroni correction is most likely due to the low power resulting from the small sample size, and the fact that the Bonferroni correction has been criticized for causing a loss of power in detecting real effects (see Glickman, 2014). It may be that due to this same issue, statistical significance was not achieved in two other *post hoc* comparisons, where the main group comparison with the Kruskal–Wallis Test reached significance (the Letter–Number Sequencing, and omissions on the left side in the bilateral trials of the Auditory dual task, Tables 6 and 13). With a larger sample size or less conservative method, there might have been a statistically significant effect between the compared pairs also in these two variables. However, when considering the main aims and findings of the present dissertation, the aforementioned possibility seems to not be crucial, because the performance in Letter–Number Sequencing was not in the main focus, and statistically significant effect in the left-sided omissions of RHS patients was reached in the bilateral trials of the Auditory dual task by analyzing the difference between omissions on the left and right sides (i.e., the Auditory dual task was sensitive too).

RT analyses of the large-screen tasks did not prove to be sensitive in identifying neglect-related symptoms. This may be due to the fact that the tasks were fast-paced and the focus was on both RTs and omissions. Choosing to focus on either of the two might have increased the diagnostic sensitivity. Because the tasks required participants to produce constant responses, as the ITI and the response window were short, it is feasible that delayed responses were classified as omissions, thus hindering the sensitivity of the RT analyses. Some previous neglect studies (Deouell et al., 2005; Rengachary et al., 2009) have deliberately attempted to increase the sensitivity of RT analyses by choosing a long response window or by replacing omissions with the longest permitted RT to improve the signal-to-noise ratio of RTs. Other studies (Andres et al., 2019; Bonato, 2015; Bonato et al., 2012, Bonato et al., 2013), on the other hand, have focused only on missed targets and increased task sensitivity by presenting brief lateral targets with a secondary task, to trigger omissions.

The present findings are partly inconsistent with some previous studies. Past studies have found that high-complexity dual tasks may induce omissions and therefore may be sensitive in diagnosing right-sided neglect in patients whose stroke is located on the left hemisphere (Blini et al., 2016; Bonato et al., 2010). In the present study, using a similar task approach, no such effect was found. Instead, in Study I, increasing the complexity of the large-screen dual task *improved* the LHS patients' reactions toward the right. One plausible explanation for this study producing different findings is that the present LHS patients did not have even subtle neglect, and, therefore, showed a similar reaction time effect in the large-screen dual task as healthy controls. This option is supported by the fact that significantly fewer LHS patients than RHS patients were clinically diagnosed as having neglect even in the early stage of recovery, and none of the dual tasks (which uncovered RHS patients' neglect and extinction) showed signs of neglect or extinction in LHS patients. It is also possible that there are some contradictions between reaction times and omissions (LHS patients' rightward bias was found in reaction times, and the aforementioned previous studies analyzed omissions). This possibility is supported by the results obtained in Study I, where the healthy controls showed faster reactions but more omissions toward the right (Tables 7, 8).

In the present studies, a combination of multiple methodological qualities was utilized, which provably increased assessment sensitivity. As the sensitivity of each of these qualities was not tested individually, the present study does not provide immediate insight into the usefulness of each individual factor. For example, in Study III, both standard and large test fields were used in the cancellation tasks but not in the dual tasks and, therefore, effect of the screen size remains elusive with respect to dual-task setting. However, a comparison of the results obtained in various test settings across Studies I-III does provide useful information. The findings obtained in the large-screen and the standard-screen settings indicate that for patients suffering from stroke in the right hemisphere, a large screen is not in itself sufficient in eliciting contralesional omissions. Conversely, a dual-task paradigm does appear to do just that. This can be observed from the standard-screen setting in running a dual task, where a significant spatial bias was observed in RHS patients, which was not detected in the large screen without the dual-task setting. As for the Ball Rain Task, there is no definitive answers regarding the influence of each individual factor in reaching the present findings, as the movement of the stimuli, the high demands for visual selective attention, or both, may well have been crucial in triggering specifically general but not (only) contralesional inattention in RHS patients. To add to this uncertainty, some previous studies have found that neglect patients' processing of moving stimuli is intact (Spinelli & Zoccolotti, 1992) and their deficits in selective attention are evident only in the contralesional hemifield (Battelli et al., 2001). Additional studies are needed to clarify this issue.

5.5 CONCLUSIONS

1) Attentionally demanding and dynamic computer methods can uncover subtle visuoattentive deficits that are not detected with traditional cancellation task approaches.

2) Distinct qualities in computer methods bring out different aspects of visual inattention: Methods that utilize moving visual stimuli and require participants to apply fast-paced selective attention bring out general inattention, whereas methods utilizing dual-task setting, central fixation point, and brief lateralized targets bring out specifically contralesional deficits.

3) To reveal subtle contralesional deficits, sensitivity of assessment can be enhanced by combining several factors that increase visual and attentional demands. In computer methods, presenting brief lateralized targets only, appears to be insufficient on its own, but when combined with a dual-task setting or bilateral targets, the necessary level of difficulty appears to be achievable. Traditional cancellation task approaches appear to be insufficient—even if the task is computerized, is presented in large perceptual space, and several other factors known to increase sensitivity are introduced.

4) Adding complexity to the visual large-screen dual task may not increase sensitivity in detecting specifically neglect-related symptoms, but may elicit a general rightward bias in reaction times.

5) Reaction time analyses may not sensitively bring out neglect-related symptoms in tasks that are fast-paced in nature and where contralesional deficits are evidenced as omissions.

5.6 CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

The present set of studies attempted to improve the assessment of mild symptoms pertaining particularly to visual attention. According to the present findings, patients with unilateral stroke may suffer from subtle visuoattentive deficits, which are not detected with traditional cancellation task approaches. Sensitive methods are needed, because the number of patients exhibiting only mild symptoms has increased as stroke treatment has progressed (Feigin et al., 2009; Jaillard et al., 2009; Jokinen et al., 2015; Kauranen et al., 2014; Mustanoja et al., 2011). At the same time, technological progress has been swift and the cognitive requirements of several facets of life have grown. Even mild visuoattentive deficits may therefore be significant in everyday situations, and critical when considering, for example, work responsibilities demanding high attention, or driving a car. Indeed, there are studies associating mild, subclinical neglect with significant real-life problems, such as colliding into objects while distracted or crashing cars on the contralesional side (e.g., Bonato et al., 2012; Deouell et al., 2005; Sotokawa et al., 2015). Additional research is needed, however, due to scarcity and inconsistency of the currently available findings. As an example, some studies, which have assessed the effects of mild neglect-related symptoms in actual traffic situations, have identified clear risks evidenced by repeated car crashes and scrapes on the car on the contralesional side, and difficulty in adequately assessing driving speed and maintaining a stable driving line (Deouell et al., 2005; Sotokawa et al., 2015). Other studies in turn have not found significant risks associated with mild neglect-related symptoms in an on-road driving test and in a follow-up interview 2 years later (Jehkonen et al., 2012). Irrespective of the risk assessment, these studies have underscored the significance of good symptom awareness and compensator skills to achieve a safe driving capability (Jehkonen et al., 2012; Sotokawa et al., 2015).

Computer methods may be useful in terms of ecologically valid assessments of driving ability, because operating a vehicle safely necessitates fast-paced visuoattentive and spatial processing, often in (large) extrapersonal space (Taylor, 2003). Traditional PnP methods are not ecologically valid in this sense because they are static and therefore not comparable to a driving setting, and are presented in a (narrow) peripersonal space. Some studies have indicated that extrapersonal and peripersonal neglect can occur independently (e.g., Cowey et al., 1994; Halligan & Marshall, 1991), stressing the importance of assessing attentional functions in both of these regions of space. The challenge from a clinical view is, however, that there are hardly any assessment methods in common clinical practice for extrapersonal neglect. Computer methods presented in a large perceptual space could offer a valid response to this demand.

As already discussed in Section 5.3, computer methods may be useful in assessing subtle general visual inattention and its manifestation together with contralesional deficits. From a clinical perspective, it is important to diagnose both deficits because their co-occurrence may exacerbate and prolong neglect symptoms (Hjaltason et al., 1996; Husain & Rorden, 2003; Samuelsson et al., 1998). Accurate and comprehensive assessment of both general and contralesional deficits may also optimize rehabilitation, because neglect can be improved by alleviating general inattention (Robertson, 2001; Robertson et al., 1995). There are yet several advantages in computer methods with respect to rehabilitation. First, computer methods can uncover mild visuoattentive deficits that are undetectable by standard PnP tests but can still cause significant real-world problems. By using computer methods, one could thus better guarantee that even patients with subclinical visuoattentive deficits will be offered rehabilitation. Second, as computer methods allow the sensitive assessment of recovery along with the diagnosis (see e.g., Bonato et al., 2012; Sacher et al., 2004), they enable the adjustment of adequate rehabilitation methods. While the patient progresses, computer methods offer a further opportunity for calibrating the task demands to a more demanding level in order to gain additional advances in assessment or rehabilitation (Bonato et al., 2010). The possibility of varying complexity, using several measures (e.g., RTs, omissions, eye movements), and presenting dynamic stimuli from different modalities (e.g., visual, auditory) increases the ecological validity and hinders the possibility of ceiling effects and compensation (Bonato & Deouell, 2013). Finally, the assessment of extrapersonal neglect, enabled by computer methods, is important—not just for the assessment of driving ability, but also for rehabilitation. Patients with extrapersonal neglect may show different kinds of real-life problems than those with peripersonal neglect (Nijboer et al., 2014a; Nijboer et al., 2014b). Patients with extrapersonal neglect perform better in basic daily activities than patients with peripersonal neglect, but are impaired in navigating (Nijboer et al., 2014a; Nijboer et al., 2014b). Therefore, separating these patients may optimize rehabilitation by allocating efforts differently to improve functional ability.

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