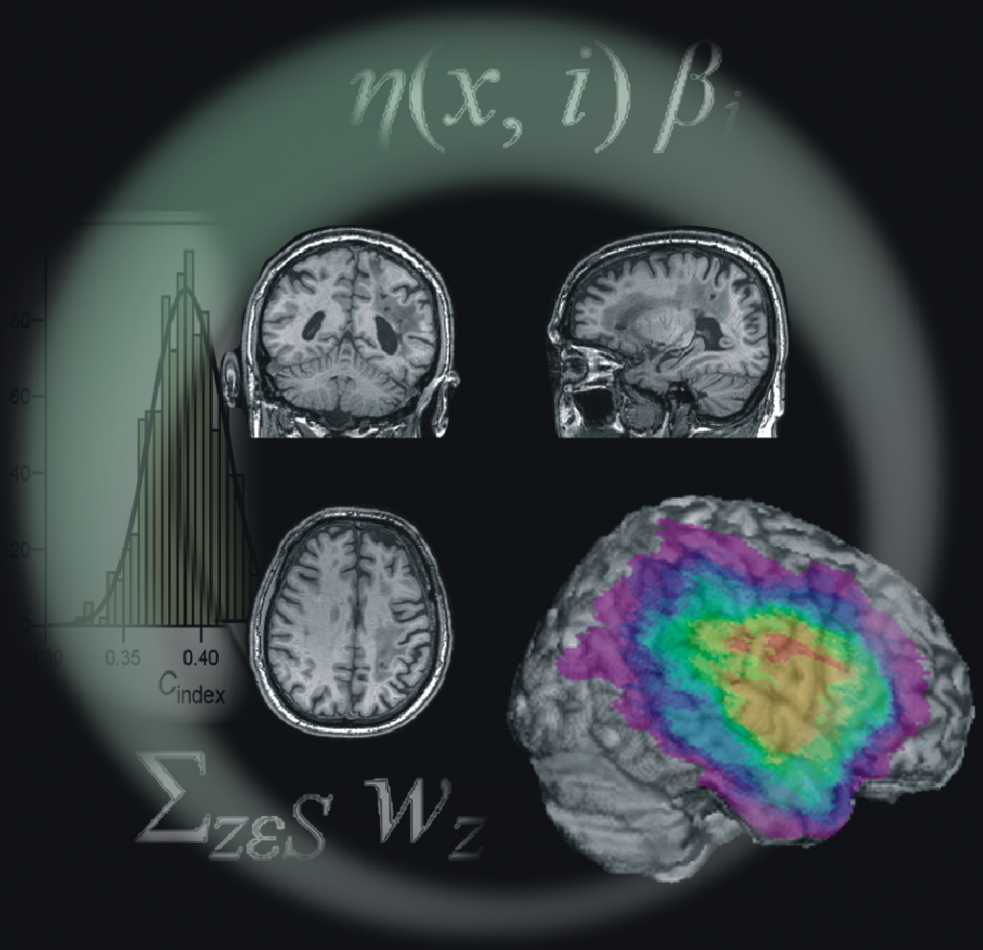
Deficits in visual attention after right side brain damage

TVA based patient studies



Ph.d. dissertation

Cand.psych. Thomas Habekost

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FOREWORD

Together with the three articles listed below, this theoretical report forms a Ph.D. dissertation in Psychology submitted to the Faculty of Social Sciences at the University of Copenhagen.

Copenhagen, 11 February 2005

Thomas Habekost

Habekost, T., & Bundesen, C. (2003). Patient assessment based on a theory of visual attention (TVA): subtle deficits after a right frontal-subcortical lesion. *Neuropsychologia, 41,* 1171-1188.

Habekost, T., & Rostrup, E. (2005a). *Persisting asymmetries of vision after right side lesions.* Manuscript submitted for publication.

Habekost, T., & Rostrup, E. (2005b). *Visual attention capacity and white matter damage.* Manuscript.

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CONTENTS

ABSTRACT

This dissertation comprises a theoretical review and three empirical articles on visual attention deficits after right side brain damage. Based on a discussion of cognitive theories it is argued that the TVA model (Bundesen, 1990) is an appropriate framework for investigating visual attention. The neural basis of visual attention is organized in large-scale anatomical networks, some of which seem lateralized to the right side of the brain. The strongest evidence for a special role of the right hemisphere comes from studies of the visual neglect syndrome. Research on neglect and other visual attention deficits is reviewed, and it is argued that these investigations would benefit from a stronger grounding in cognitive theory. A method of patient assessment based on TVA is reviewed and developed. The method was applied in three empirical investigations. The first study (Habekost & Bundesen, 2003) demonstrated the sensitivity and specificity of the method in a single case with minor clinical symptoms. In the second study (Habekost & Rostrup, 2005a) the method was applied for a large-scale investigation of visual asymmetries after right side lesions. The third study (Habekost & Rostrup, 2005b) showed the importance of posterior white matter damage for general deficits in visual attention capacity. The contributions of the Ph.d.-project to neuropsychological theory are summarized and discussed.

DANSK RESUMÉ

Denne afhandling indeholder en teoretisk oversigt samt tre empiriske artikler om visuelle opmærksomhedsforstyrrelser efter skade i højre side af hjernen. Med udgangspunkt i en diskussion af kognitive teorier argumenteres der for, at TVA modellen (Bundesen, 1990) er en velegnet ramme til undersøgelser af visuelle opmærksomhedsforstyrrelser. Den neurale basis for visuel opmærksomhed er organiseret i større anatomiske netværk, hvoraf nogle synes lateraliseret til den højre side af hjernen. Den stærkeste evidens for en særlig betydning af den højre hjernehalvdel kommer fra undersøgelser af det visuelle neglektsyndrom. Forskning i neglekt og andre opmærksomhedsforstyrrelser gennemgås, og der argumenteres for at disse undersøgelser ville styrkes af en bedre rodfæstning i kognitiv teori. En metode til patientundersøgelser baseret på TVA gennemgås og udvikles. Metoden blev anvendt i tre empiriske studier. Det første studie (Habekost & Bundesen, 2003) demonstrerede metodens sensitivitet og specificitet i en enkelt patient med kun mindre kliniske symptomer. I det andet studie (Habekost & Rostrup, 2005a) blev metoden anvendt til en større undersøgelse af visuelle asymmetrier efter højresidig skade. Det tredje studie (Habekost & Rostrup, 2005b) viste betydningen af skade i den posteriore hvide substans for generelle reduktioner i visuel opmærksomhedskapacitet. Ph.d.-projektets bidrag til neuropsykologisk teori opsummeres og diskuteres.

1. INTRODUCTION

Every second the brain is presented with a challenge. The sensory receptors deliver a massive, constantly changing set of inputs, from which only the most important must be chosen for consciousness and response. In case of vision the task is particularly complex. The visual field is typically filled with objects that each requires extensive analysis to be recognized. From moment to moment, the brain must pick the most significant objects and direct its resources there - otherwise we would be flooded by information. Luckily the brain is remarkably good at this job, and under most circumstances we do in fact focus on what is relevant and respond appropriately. Presumably the brain can accomplish this feat only because numerous anatomical regions are involved in visual processing, and because the function of these regions is integrated in complex, but highly effective networks. However for some individuals this fine machinery is disturbed. Because so many cerebral areas are related to vision, brain injury often affects the function in some way. This may lead to absolute deficits, as when primary visual pathways are damaged and the person becomes blind, but more subtle problems also occur. When higher parts of the visual system are damaged the person may still be able to see, but the efficient selection and recognition that characterizes the healthy brain is often compromised. Many such disturbances can be described as visual attention deficits, and it is these less obvious effects of brain damage that form the subject of the present work.

The general aim of the thesis is to explore the cognitive structure and lesion anatomy of visual attention deficits after brain damage. Central to this effort is a recently developed method of patient assessment based on a theory of visual attention

(TVA; Bundesen, 1990). TVA is a model of normal cognition and strongly grounded in basic cognitive research. By using this theoretical framework the investigations differ from most previous studies of visual attention deficits, which have been conducted in a neuropsychological tradition that emphasizes marked clinical deficits. However it is a basic claim of the thesis that TVA based assessment holds several advantages to the conventional approach. First, the method can reveal deficits that are not evident in standard clinical examination (sensitivity). Second, performance is analyzed into separate functional components (specificity). Third, these components are not specific to the tasks used, but reflect general aspects of visual attention (validity). Fourth, the measurement error related to each test result can be directly quantified, and in most cases shown to be minor (reliability).

Although TVA based assessment is relevant to many types of brain injury, the present investigation is confined to strokes in the right side of the brain. Besides the inherent limitations of a Ph.d.-project, there are several reasons for this selection. Stroke produces relatively circumscribed lesions, which makes this type of brain damage well suited for mapping links between anatomy and function. Moreover, stroke is a very common type of brain injury with obvious clinical relevance. Strokes generally affect only one side of the brain, and several lines of evidence suggest that the right hemisphere plays a special role in visual attention. The Ph.d.-project sets out to characterize the attentional function of this side of the brain in greater detail.

Potentially, a study of visual attention deficits can bring about two types of knowledge. It can advance clinical understanding by showing effects of particular types of brain damage. Such knowledge forms the basis of practical assessment and rehabilitation of patients. However, by showing which anatomical structures are critical

for a particular function, lesion studies can also inform research on the healthy brain. The present thesis aims to contribute in both these respects, and address clinical as well as general topics of neuropsychology.

2. COGNITIVE THEORIES OF VISUAL ATTENTION

Attention is a general term for selectivity in perception (Bundesen & Habekost, 2005). A wide range of cognitive phenomena are subsumed under this definition, and many different aspects of attention have been studied. Despite this diversity most theories agree on some general characteristics, most notably limited capacity and selectivity, as central to the concept of attention. However significant controversy remains over specific properties of the function, for example whether selection occurs early or late in processing, if it is spatial or object based, and how selection is controlled. Perhaps the most fundamental disagreement concerns whether attention works in a mainly serial or parallel way. A comprehensive theory of attention should address all of these issues.

Since modern attention research was pioneered in the 1950s, most theories have been based on performance in visual tasks. Substantial progress has been made on many issues (Logan, 2004), and the present investigations of visual attention can thus be grounded in a relatively advanced field. This chapter presents highlights of research on visual attention, introduces the TVA model, and evaluates its merits in the context of basic cognitive theory.

2.1) Central issues

In an early treatment of the subject James (1890/1950) identified two key properties of attention: limited capacity and selectivity. James' basic description of attention is still widely accepted (and, partly due to the quality of his prose, quoted in most introductions to the subject). However modern research on attention has greatly elaborated on the details of the function. Separate types of capacity limitations have

been identified and modelled quantitatively. Especially the selective process, which is at the heart of attentional function, has been the subject of intense research. In general, investigators have sought to determine *when* selection occurs in the processing of visual stimuli, *what* is selected, and *how* selection comes about, including how it is controlled by the subject. Under the headings of vigilance and sustained attention, fluctuations in attentional function have also been studied. The following section provides an overview of these central issues in attention research.

Limited capacity

Despite the massively parallel architecture of our visual system, there are strong limitations on the number of objects we can recognize at the same time. Accordingly, nearly all theories of visual attention assume that capacity is limited (Atkinson, Holmgren, & Juola, 1969; Broadbent, 1958; Bundesen, 1987; Treisman & Gelade, 1980; but see van der Heijden, 2004). Indeed, limited perceptual capacity is often proposed as the explanation why attentional selectivity is needed (e.g., Mesulam, 1985). However limited capacity and selectivity may have evolved for a number of neurophysiological and functional reasons (see Cowan, 2001).

The limited capacity of the visual system has been investigated in divided attention tasks, where subjects attend to multiple stimuli at the same time. Two main types of limitation have been identified. One is related to the storage capacity of visual short-term memory (VSTM) (Baddeley, 1986; Cowan, 2001), whereas the other reflects limits in processing speed (Shibuya & Bundesen, 1988). Classical studies were conducted by Sperling (1960, 1967) on the information available in brief visual presentations. Sperling (1960) used a whole report task, in which the subject was

instructed to report as many items as possible from a brief display (see section 5.1 for a detailed discussion of this paradigm). The experiment showed that a maximum of about four unrelated items could be reported. This finding has been replicated several times (Bundesen, Pedersen, & Larsen, 1984; Shibuya & Bundesen, 1988; present thesis) and can be interpreted as a reflection of the maximum storage capacity of VSTM (Sperling, 1967). The visual storage limitation of about four objects has also been found in change detection paradigms (Vogel, Woodman, & Luck, 2001). There is evidence that storage capacity is limited only in terms of integrated objects rather than the number of features within objects (Luck & Vogel, 1997), but this has recently been questioned (Alvarez & Cavanagh, 2004).

Sperling's whole report studies also revealed a second type of capacity limitation. Until reaching the ceiling of about four items, the number of correctly reported items improved with increasing exposure duration. The pattern suggested that besides VSTM storage capacity there was a limitation in the visual encoding rate. This conclusion was supported by an analysis of similar data by Shibuya and Bundesen (1988). They argued that if processing capacity was unlimited, the initial rate of increase of the mean score function (where storage capacity limitations are negligible) should be proportional to the number of items in the display. Instead their data suggested that the initial rate of increase was essentially constant across display sizes, consistent with the hypothesis that total processing capacity was fixed. Studies of the limitation in visual processing capacity are still sparse, perhaps because its effect is difficult to separate from the VSTM limitation. However the TVA model provides a method for this analysis (see chapter 5).

Another famous finding by Sperling (1960) was evidence for a very short-lived sensory memory of unlimited capacity (*iconic memory*). Within a few hundred ms after the (unmasked) stimuli had vanished, subjects could access most of the information in the display. After this brief period, the VSTM limitation of about four items applied. In general, most theories assume that attentional selection is supported by "preattentive" or "automatic" processes with unlimited capacity. Typically these processes are thought to provide an initial sensory analysis of the visual field (cf. FIT, FIRM, and Guided Search theories, section 2.2).

The locus of selection

The first modern theory of attention, Broadbent's filter theory (1958), asserted that unattended stimuli were analyzed only in terms of simple physical features (i.e., blocked at an early stage of processing). This view was challenged by Deutsch and Deutsch (1963), who proposed that attended and unattended objects receive the same amount of processing by the recognition system. Only after stimuli have been recognized are their importance retrieved, and some selected for consciousness and response. These are classical examples of "early" and "late" selection theories. The point of controversy is whether stimuli are selected before or after pattern recognition. During the next decades this discussion remained central to attention research (Duncan, 1980; Shiffrin & Schneider, 1977; Treisman, 1964a, 1964b; Treisman & Gelade, 1980). In particular the question was examined in experiments featuring automatic interference from distracting elements, such as the Stroop paradigm, Eriksen's flankers task, and negative priming experiments. Evidence for both semantic ("late") influence of distracters (Driver & Tipper, 1989; Eriksen & Eriksen, 1974; Fox, 1995) and efficient ("early") filtering of

distracter elements (Paquet & Lortie, 1990) were reported. Lavie (1995) proposed a theory to accommodate the mixed set of findings, in which processing of distracter objects depends on the perceptual load of the task. If perceptual load is low, distracters are processed automatically, giving rise to interference effects (late selection). However if perceptual load is high, distracters receive little processing (early selection). Other researchers claim that the question of early versus late selection is ill posed (Allport, 1993), and instead of viewing attentional selection and object recognition as two separate processing stages, they should be seen as two aspects of the same process (simultaneous selection; Logan, 2002).

What is selected?

Closely related to the issue of early versus late selection is the question of whether attention is directed to segmented objects or to regions of space. If the initial (preattentive) analysis of the visual field operates at the level of simple physical features, attentional selection cannot be based on integrated, high-level representations (i.e., objects). Instead, many theories assume that particular regions of space are selected for enhanced processing. This corresponds to the classic spotlight metaphor for attention (Posner, 1980), where attention functions like an "inner eye" that scans the visual field in serial manner (see also section 2.2). Main support for this view has come from studies of spatial cueing (Posner & Cohen, 1984; Posner, Nissen, & Ogden, 1978; Posner, Snyder, & Davidson, 1980), where the subject's attention is drawn to specific parts of the visual field (without moving the eyes: covert attention) before the target stimulus appears. Relative to a neutral condition, cueing to a different location than the target gives rise to *costs* in reaction time, whereas cueing to the same location produces

benefits. A traditional interpretation of these findings is that attention is first engaged at the cued location, and has to be disengaged and moved if the target appears in another location (Posner, Walker, Friedrich, & Rafal, 1984).

However much evidence now suggests that attention cannot be based entirely on spatial criteria (Driver & Baylis, 1998). Visual elements that form groups according to Gestalt laws tend to be selected together, and divided attention is more effective within an object than across objects (also when the objects are placed in overlapping positions). Accordingly, object-based theories of attention (Duncan, 1984; Neisser, 1967) assume that preattentive analysis segments the visual field into Gestalt-grouped objects, which then form the basis of selection. Acknowledging the validity of both views, current theories tend to integrate both spatial and non-spatial mechanisms (e.g., Humphreys, 1999; Logan, 1996).

Whether selection is conceived as spatial or nonspatial, most theories do not specify how the attended object is categorized. However, given that many categorizations are always possible for a given physical object, categorization is also a choice process. Broadbent (1970, 1971) introduced a general distinction between two selective mechanisms in attention: *filtering* and *pigeonholing* (see also Duncan, 1985; van der Heijden, 2004). Filtering determines which objects are selected (stimulus set), whereas pigeonholing concerns how the selected objects are categorized (response set). Both mechanisms seem necessary for efficient attentional function.

Attentional control

Already Leibniz (1765/1996) distinguished between two basic aspects of attention: passive, automatic capture by salient objects, and active, voluntary concentration. This

distinction has been preserved in modern cognitive theories under the headings of bottom-up and top-down control of attention. A large empirical literature now exists on these two types of mechanisms and their interaction. Bottom-up influences on attention has been studied by experiments featuring attentional capture by salient objects (e.g., a green object among red ones) and abrupt onsets (Theuwes, 1996; Yantis, 1998), often showing strong effects. However attentional capture probably does not occur in a completely automatic way, but rather interacts with (top-down) attentional control settings (Folk, Remington, & Johnston, 1992) such that certain types of attentional capture (e.g., abrupt onsets) can be given priority. The efficiency of top-down control has been examined in partial report experiments, where target objects characterized by a certain feature must be recognized in the presence of distracters (Bundesen, Shibuya, & Larsen, 1985; Duncan, 1985; Shibuya, 1993; see also section 5.1). Other paradigms that feature interference from distracting elements are the Stroop test, Eriksen's flanker task, and negative priming. Top-down control of selection is generally imperfect, except perhaps under conditions where uncertainty about the upcoming target is minimized (e.g., Paquet & Lortie, 1990).

Controlled selection can be automatized after consistent practice, such that objects previously selected by top-down mechanisms start to capture attention involuntarily (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). Automatization of controlled processes was a central topic of attentional research in the 1970s, and the related topic of executive attention has recently moved to the front of attentional research, particularly in the form of task switching studies (Logan, 2004). Executive attention represents the complex aspects of top-down control that come into play under response conflict or in novel situations. In terms of formal theories of attention,

executive functions determine parameter values that control the (automatic) function of lower levels in the system (e.g., Logan & Gordon, 2001). Related to this concept is the notion of a central executive (Baddeley, 1986) that controls subordinate processes. However as one moves up in the control hierarchy of psychological processes, the spectre of an extra-theoretical homunculus gradually emerges: What controls the highest level described in the model? Short of metaphysic discussions on the nature of free will, a pragmatic strategy towards this problem is to gradually reduce the relevance of the homunculus by providing mechanistic descriptions of still more processes. The TVA model and its extensions can be viewed as a highly developed example of this approach (see section 2.3).

Sustained attention

Cohen (1993) made a distinction between two types of limitation in attentional capacity: *structural* and *energetic*. Structural limitations determine the maximal processing ability of the individual, and reflect inherent properties of the cognitive system. However due to fluctuations in motivation and other "energetic" factors, the maximal level of performance can be difficult to sustain over longer periods of time. The *vigilance* aspect of attention has been studied in monotonous "watchkeeping" tasks (Robertson & Manly, 1999). A general finding in these tasks is that over time detection rates tend to decrease and reaction times tend to increase (vigilance decrement; Parasuraman, Warm, & Lee, 1998). Early studies suggested that the decrement was caused by a gradual shift towards more conservative response criteria (Broadbent, 1971), but later investigations also showed declines in target sensitivity (Davies & Parasuraman, 1982). Fisk and

Schneider (1981) made the point that if the task is highly automatized (i.e., demands little attention), performance typically remains high.

Compared to structural limitations of capacity, energetic factors have been poorly integrated in mainstream cognitive research on attention (Bundesen & Habekost, 2005; Cohen, 1993), and sustained attention has been viewed more as a source of error than an object of study in itself. Therefore studies of vigilance to a large extent remain a separate line of research. However neural aspects of the function are quite well investigated under the concept of cortical arousal. General arousal systems have been identified in the brain (see chapter 3) and related to neuropsychological syndromes such as neglect (see chapter 4).

2.2) Serial and parallel models of attention

The previous section outlined a range of issues that any comprehensive theory of visual attention should address. Among such general theories of visual attention, a major division line runs between serial and parallel models (Bundesen & Habekost, in press). Besides the central importance of the serial-parallel issue, models in the same group tend to agree on other basic issues. This makes it useful to organize a review of attention models around this topic.

In serial models only one stimulus is attended at a time. Intuitively this notion is related to the metaphor of a spotlight that moves across the visual field, focusing on single elements in sequence (Posner, 1980). In a typical serial model of attention, selection is spatially defined and only the currently attended object receives high-level processing (i.e., selection occurs early). Serial models of attention traditionally depend heavily on findings from visual search experiments. In the most

common form of this paradigm, the subject is presented with a display that contains either a single or no target objects, along with a varying number of distracter items. The task is to respond as soon as the target is detected (positive reaction), or when it is obvious that no target is present (negative reaction). Two fundamental types of visual search were described by Treisman, Sykes, and Gelade (1977): feature and conjunction search. In feature search, the target object is characterized by a simple "physical" feature (e.g., a particular colour, size, or curvature) that none of the distracter items possess. Due to its unique feature value, the target immediately seems to "pop out" of the display, and search times are little effected by the number of distracters (the display size). In conjunction search, the target is characterized by a specific combination of features (e.g., a particular colour and a particular shape), but is not unique in any of the component features of the conjunction. In this case search for the target object is effortful, and reaction time (RT) usually increases linearly with display size. Specifically (when a general latency component is subtracted from the RT) the RT to a display that contains a target is about half as long as to a display in which the target is absent. In other words, when RT is plotted as a function of display size, the ratio between the slopes of positive versus negative RT functions is 1:2. Much of attention research in the 1980s revolved around visual search (Logan, 2004), and many of the basic findings (such as the 1:2 RT ratio) fit well with serial models. In the process of accounting for more complex patterns of data, serial models have progressed from simple to selective models. This theoretical development is traced in the following.

By simple serial models, items are scanned one by one, and the order in which items are scanned is random (i.e., non-selective). The most prominent example of a simple serial model is the *Feature Integration Theory* (FIT; Treisman & Gelade,

1980), which was probably the dominant theory of attention in the 1980s. The background for FIT was neurophysiological findings that showed a strong modularity in the processing of visual input (for a review see Zeki, 1993). For example, qualities like colour, form and motion seemed to depend on separate regions of extrastriate cortex. This pushed the *binding problem* to the forefront of visual research: How are these separate features unified to form whole objects in our phenomenal experience? FIT proposes (spatial) attention as the integrating mechanism. According to FIT, elementary visual features are registered automatically (i.e., without attention) and in parallel across the visual field. This makes it possible to determine preattentively whether a particular feature is present in the visual field, and explains why feature search does not depend on the display size (i.e., can be carried out in parallel across the visual field). The results of the parallel evaluation of the visual field are stored in separate maps for each feature type. Each of these feature maps is organized retinotopically (i.e., such that the spatial arrangement of stimulation on the retina is preserved). The core assumption of FIT is that spatial attention is necessary to bind individual features into representations of whole objects. The integration is produced by an attentional spotlight that moves within a *master map of locations* and selects the currently represented features at the attended location. The selected features are bound together to form an object, which then receives high-level processing (recognition). After binding the features, the attentional spotlight moves to another location, and a new recognition process is initiated. The serial scanning process is assumed to occur at a very high rate, typically estimated at around 50 ms or less per item. In conjunction search objects are attended one at a time, and if no target is present all items in the display must be attended before a response can be made. If a target is present, on average half of the display objects are scanned before

the target is detected (since selection is random). This provides a simple explanation for the 1:2 ratio of RT slopes mentioned above. However it has been pointed out that parallel mechanisms of search can also produce a positive-to-negative RT slope of 1:2 (Pashler, 1987). In addition, it gradually became apparent that visual search experiments do not show a clear division between (parallel) feature search and (serial) conjunction search (Wolfe, 1998). Rather, the efficiency of visual search seems to be a continuous function of the similarity between items in the search display (Duncan & Humphreys, 1989).

FIT was later revised into a selective serial model of attention (Treisman & Sato, 1990). By selective serial models, the order of scanning is determined by an initial, pre-attentive analysis of the whole visual field. This improves the efficiency of visual search so that fewer items have to be attended before a target is discovered, avoiding the assumption of very high scanning rates (cf. simple serial models). Early studies suggested that such rates are implausible (Colegate, Hoffman, & Eriksen, 1973), which has been confirmed by much research in the 1990s (see end of section). The most influential example of a selective serial model is the *Guided Search* theory of Wolfe and associates (1989, 1994). The Guided Search model employs the same basic two-stage mechanism as FIT. In the first stage, simple features are registered pre-attentively and in parallel across the visual field. In the second stage, attention is focused serially at each object to enable visual recognition. However, unlike FIT, the outcome of the first stage of analysis guides the processing at the second stage. The parallel stage produces a general activation map of the visual field (saliency map; cf. Koch & Ullman, 1985; Bundesen, Habekost, & Kyllingsbæk, in press) which represents the probability that the object at each location is a target. The activation in the saliency map is determined by

both bottom-up and top-down factors. The parallel stage suggests probable targets by way of the saliency map, but the evaluation is prone to error and serial processing is necessary for definite classification of the object. For this purpose objects are processed (attended) one by one in order of decreasing activation in the saliency map. To ensure that a rejected item is not checked again its activation value is lowered, and the search process thus contains a memory function. The serial search stops when a target is detected or when all items with activations above a certain value have been processed. Like FIT, Guided search is mainly supported by findings on visual search, and provide close fits to many results (Wolfe, 1994). However the Guided Search model cannot account for several fundamental results (Bundesen & Habekost, 2005). In particular, the 1:2 ratio of positive-to-negative reaction time slopes in conjunction search is not predicted. This data pattern requires that serial selection is random or "un-guided" (Bundesen, 1998) as in simple serial models: If search is guided, one should on average have to search less than half of the display to find a target. The Guided Search theory also has difficulty accounting for data from experiments in which all items are targets (i.e., whole report) and selectivity is irrelevant. If these data are to be fit by a serial model, they require (implausible) assumptions of very rapid attentional shifting. Finally, Wolfe himself provided evidence against a basic assumption of the model: that scanned items are marked to prevent rechecking. Horowitz and Wolfe (1998) found that visual search rates were unaffected by prior experience with the display, which showed that information did not accumulate during the process (memory-less search). Instead the finding is consistent with parallel models in which processing times of visual objects are exponentially distributed (e.g., the FIRM model; see below). The exponential

distribution implies that the probability that an event occurs is completely independent of prior events (i.e., a memory-less process).

In parallel models of attention, several stimuli can be attended at the same time. Parallel models typically (but not necessarily) assume late selection, as well as the importance of nonspatial selection criteria. Like serial models, parallel models have undergone a theoretical evolution from simple to more complex (limited-capacity and race-based) accounts. In simple parallel models, processing times for individual stimuli are statistically independent, and capacity is unlimited (e.g., Eriksen, 1966). These models account well for visual search tasks where selection is highly efficient (e.g., feature search), but cannot explain the linear relation between mean reaction time and display size found in more difficult search tasks. However this finding can be accommodated by parallel models with limited processing capacity (Atkinson et al., 1969; Townsend, 1969). A particular class of limited-capacity parallel models is race models, where attentional selection is determined by the temporal properties of processing: The items that first finish processing are selected.

An important race model is the Fixed-Capacity Independent processing Model (FIRM) proposed by Shibuya and Bundesen (1988; see also Bundesen, 1987; Shibuya, 1993). FIRM assumes that the parallel processing of a visual display occurs in two stages. First an attentional weight is computed for each item in the display, based on the sensory evidence that the object is a target. Then a fixed total processing capacity is distributed among the display items according to their relative attentional weights. The amount of capacity allocated to an item determines how fast it is processed. Each item races the others for a few available slots in VSTM, and the time taken to process each item follows an exponential distribution with a rate parameter equal to the amount

of processing capacity allocated to the item. The predictions of FIRM were subjected to very detailed testing in a partial report experiment (which also included conditions with no distracters, i.e. whole report). Figure 1 shows the score distribution of an individual subject along with the data fit by FIRM. Four parameters were used to model the data: C (processing capacity), K (storage capacity of VSTM), α (ratio of the attentional weight of a distracter to the weight of a target), and t_0 (minimum effective exposure duration). As can be seen, the fit is extremely close, taken into consideration the complexity of the distribution and the few parameters used to model it. The parameter values used to fit the distribution were: K = 3.7 objects, C = 49 objects / second, α = 0.4, and t_0 = 19 ms, all of which are plausible. Shibuya and Bundesen (1988) and Shibuya (1991) compared the fit to alternative serial and parallel models, and consistently found that the fits provided by FIRM were superior.

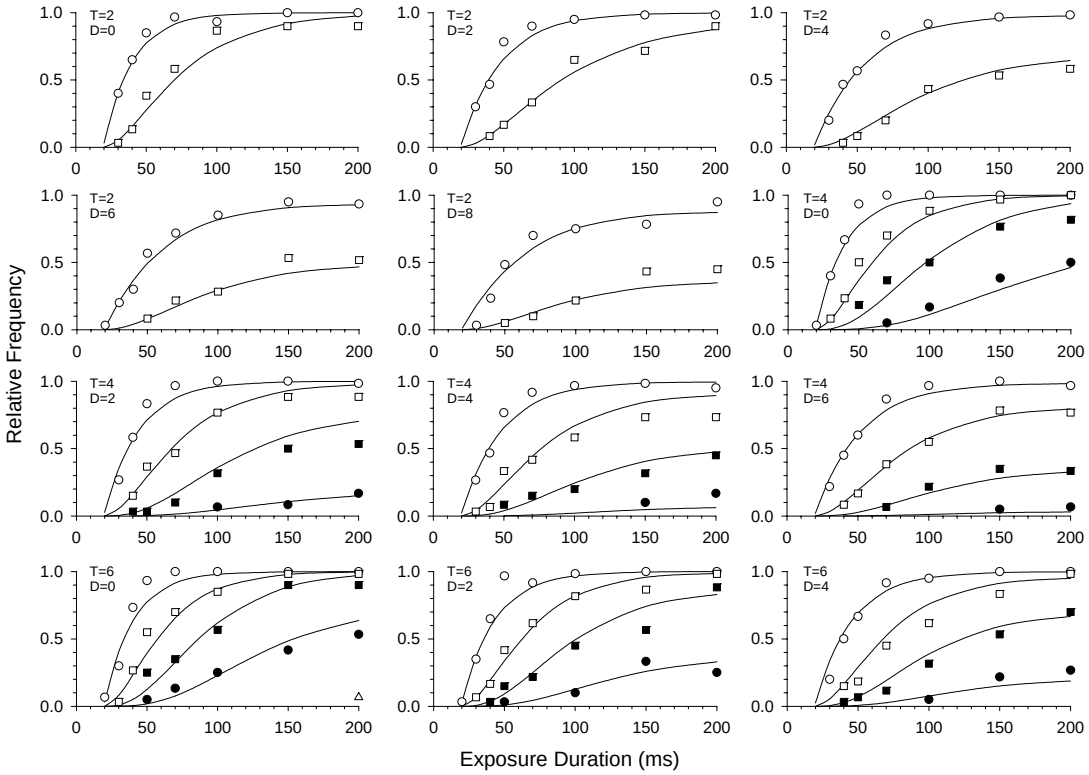

Figure 1. *Relative frequency of scores of j or more (correctly reported targets) as a function of exposure duration with j, number of targets T, and number of distractors D as parameters in the partial report experiment of Shibuya & Bundesen (1988). Data are shown for subject MP. Parameter j varies within panels; j is 1 (open circles), 2 (open squares), 3 (solid squares), 4 (solid circles) or 5 (triangle). T and D vary among panels. Smooth curves represent a theoretical fit to the data by the FIRM model (Adapted from Bundesen & Habekost, 2005).*

Serial models typically predict very rapid attentional shifting (e.g., every 50 ms), at least if all items are targets. In contrast, parallel models often assume an *attentional dwell time* of several hundred milliseconds, during which a particular distribution of processing resources is maintained (which can imply processing of several objects simultaneously). In the last decade the latter view has received strong support from two sources: attentional blink experiments and neurophysiological data. The attentional blink refers to the phenomenon that when two targets are presented sequentially within about 500 ms of each other, report of the second target is markedly

impaired (Shapiro, Raymond & Arnell, 1994; Weichselgartner & Sperling, 1987). This was perhaps the most intensively studied effect in attentional research of the 1990s, and the results generally support the notion of a long attentional dwell time (Ward, Duncan, & Shapiro, 1996). In addition, single cell studies in monkeys point to attentional effects on the same time scale (Chelazzi, Duncan, Miller, & Desimone, 1998; Chelazzi, Miller, Duncan, & Desimone, 1993).

Today the most influential parallel model of attention is perhaps the *biased competition* theory by Desimone and Duncan (1995; see also Duncan, 1996, 1999). The biased competition theory has been very successful at integrating findings from neuroscience, in particular single cell studies of attention (see section 3.2). Similar to FIRM, it is assumed that objects in the visual field initially activate many representations (brain systems) in parallel, and that these representations compete for control of consciousness and response. However selection is not conceived as an independent race between objects, but rather as a mutually inhibitive process in which features of the same object reinforce each other while suppressing activations of other objects. Over the course of a few hundred milliseconds (cf. the attentional dwell time), the cognitive system is assumed to reach a stable state in which activations belonging to one object dominate throughout (winner-takes-all selection; see also Phaf, van der Heijden, & Hudson, 1990). The selection process is biased in the sense that objects with particular, high-priority features compete with greater strength. The biased competition theory is an object-based model of selection, and many properties besides spatial location can receive priority by the system (e.g., colour, shape, and complex conjunctions of features). The TVA theory is in many ways similar to the biased competition model, and has now also been interpreted at the single cell level (Bundesen,

Habekost, & Kyllingsbæk, in press). However TVA is mathematically formal, and there are also substantial differences between the proposed selection processes in the two theories. These differences mainly concern the question of independent processing and whether there are separate selection mechanisms for objects and categorizations.

2.3) A theory of visual attention (TVA)

Bundesen (1990) presented a unified theory of visual recognition and selection: TVA. TVA combines a choice model for selection from multi-element displays (Bundesen, Pedersen, & Larsen, 1984) that was developed into a race model (FIRM; Bundesen, 1987; Shibuya & Bundesen, 1988) with the *biased-choice* model for single-stimulus recognition (Luce, 1963; Shepard, 1957). The TVA theory itself has been generalized to include spatial effects (CTVA; Logan, 1996) as well as executive function (ECTVA; Logan, 2001) and effects of memory and categorization (ITAM; Logan & Gordon, 2002). Here the model is presented in its original form, which formed the basis of the empirical investigations of this dissertation.

Unlike most other theories of attention TVA is quantitatively explicit. Whereas for example FIT and the biased competition theory describe attentional selection in a schematic way, TVA includes a mathematical description of the time course of the process. A fundamental assumption of TVA is that visual processes are best modelled using stochastic rather than deterministic principles. Accordingly, TVA predicts the probability that an event (e.g., visual recognition of an object) will occur during a specified time interval. In comparison to deterministic models, which assume that cognitive processes have no variability, this approach affords much more power to describe the complexities of perception and attention (Townsend & Ashby, 1983).

In TVA, both visual recognition and attentional selection consist in making *visual categorizations* of objects. Objects are defined as perceptual units in the sense of Gestalt theory. Formally, categorizations have the form "object *x* has feature *i*". A categorization is made (selected) if and when it enters a limited-capacity short-term store (VSTM). The storage capacity of VSTM is limited to *K* objects (about 3-4 in normal observers, cf. section 2.1), but not in terms of the number of categorizations that can be made of objects already encoded (cf. Luck & Vogel, 1997). Visual categorizations are processed mutually independent and in parallel, and processing is organized as a race towards VSTM. This means that selection is determined by the temporal characteristics of processing: The objects that are selected are those objects whose encoding processes complete before the sensory representation of the display vanishes, provided that VSTM has not been filled up with other objects.

Consider the time taken to process a given categorization "element *x* has feature *i*". As explained above, processing time is a stochastic variable following a probability distribution. This distribution is defined by the hazard function of the categorization (i.e., the conditional probability density that the perceptual categorization finishes processing at or before time *t*, given that the categorization has not finished processing before time *t*). In TVA the measure is called the *v* value of the categorization, in this case "object *x* has feature *i*", $v(x,i)$. $v(x,i)$ is determined by two basic equations, which form the core of the TVA theory. By the first equation,

$$v(x, i) = \eta(x, i)\, \beta_i\, w_x / \Sigma_{z \varepsilon S}\, w_z. \qquad (1)$$

where $\eta(x,i)$ is the strength of the *sensory evidence* that element x has feature i, β_i is the perceptual bias associated with feature i, S is the set of elements in the visual field, and w_x and w_z are *attentional weights* for elements x and z, respectively. The attentional weights are derived from *pertinence* values that reflect the current importance of attending to objects belonging to certain categories (processing priority). The attentional weight for each element x in the visual field is given by the second equation of TVA:

$$w_x = \sum_{j \varepsilon R} \eta(x, j)\, \pi_j. \quad (2)$$

where R is the set of all perceptual categories, $\eta(x,j)$ is the strength of the sensory evidence that element x has feature j, and π_j is the pertinence value of category j. In tasks where the participant is required to focus on target objects rather than distracters, attentional weights should be higher for targets than distractors. The ratio between the weight of a distracter and a target is a measure of the efficiency of selection, denoted α:

$$\alpha = w_{\text{distractor}} / w_{\text{target}}. \quad (3)$$

In other contexts it is relevant to compare the attentional weights of (target) objects in different parts of space. This can be done by computing a relative index (w_{index}) for attentional weights. For example in case of left versus right side comparisons:

$$w_{\text{index}} = w_{\text{left}} / (w_{\text{left}} + w_{\text{right}}). \quad (4)$$

where w_{left} is the attentional weight of a target in the left visual field, and w_{right} the weight of a right side target. By equations 1 and 2, v values depend on η, β, and π values. In most experimental tasks, these parameters can be assumed constant during the stimulus presentation. This implies that v values are also constant. Since v values were defined as hazard functions, this means that processing times for visual categorizations are exponentially distributed with rate parameters given by v. The rate parameter can be described as the "speed" with which a categorization of an element races towards VSTM. In case of a single object x in the visual field, the probability p_x that the object finishes processing (i.e., is encoded into VSTM) at time t is given by:

$$p_x = 1 - \exp\,[-v_x * (t - t_0)\,]. \qquad (5)$$

t_0 denotes the minimal effective exposure duration (visual threshold), below which information uptake is assumed to be zero, and the equation presupposes that $t \geq t_0$. The difference $(t - t_0)$ is the *effective exposure duration* of the stimulus display. If the stimulus is unmasked, an additional effective exposure duration of μ ms is added.

The total processing capacity C for any given display is defined as the sum of v values across all perceptual categorizations and elements in the visual field:

$$C = \sum_{x \varepsilon S} \sum_{i \varepsilon R} v(x, i). \qquad (6)$$

If the sensory effectiveness for all elements in the display is equal, C is constant across variations in both the number of objects in the display and their attentional weights (for a proof, see Bundesen, 1990). However in studies of brain damage, sensory

effectiveness often cannot be assumed equal across the visual field. In this case, separate values of C are estimated in the relevant parts of space.

Following Broadbent (1970, 1971), TVA includes two selection mechanisms: filtering and pigeonholing. Whereas filtering affect which objects are selected, pigeonholing determines how these objects are categorized. Filtering is controlled by pertinence (π) values, which determine attentional weights and thereby the probability that any categorization from a given element will enter VSTM. Pigeonholing depends on bias (β) values and modulates the probability that a particular categorization is made, independent of which object is selected.

Bundesen (1990) used the TVA model to obtain close quantitative fits to many of the central experimental findings in the attention literature. Being a generalization of the biased-choice model and the FIRM race model, TVA inherited the success of these models at describing findings from single-stimulus recognition (Luce, 1963; Townsend & Ashby, 1983), whole report (Sperling, 1960, 1967) and partial report (Bundesen et al., 1984, 1985; Shibuya & Bundesen, 1988). In studies of divided attention, TVA accounted for findings on object integrality in selective report (Duncan, 1984), cued detection (Posner et al., 1978), and target redundancy (van der Heijden, La Heij, & Boer, 1983). In studies of focused attention, the theory accounted for performance in conjunction and feature search (Treisman & Gelade, 1980), search with perceptual grouping (Bundesen & Pedersen, 1983), selective detection (Estes & Taylor, 1964), shifting of the attentional focus (Colegate et al., 1973), and effects of consistent practice in search (Shiffrin & Schneider, 1977; Schneider & Fisk, 1982). Since the 1990 paper, central assumptions of TVA concerning stochastic independence between categorizations (Bundesen, Kyllingsbæk, & Larsen, 2003) and exponential distribution

of processing times (Bundesen & Harms, 1999) have been confirmed. Further, in their review of the attention literature Bundesen and Habekost (2005) extended the coverage of TVA to explain findings on attentional capture (Folk et al., 1992) and memory-less search (Horowitz & Wolfe, 1998). TVA's most important success in recent years has been to account for a large part of the single cell studies of visual attention (Bundesen et al., in press). Being strongly constrained at both the psychological and single cell level, TVA may now be said to bridge cognitive and neurophysiological theories of attention.

Besides accounting for a wealth of empirical findings, TVA addresses most of the theoretical issues in visual attention research outlined in section 2.1. The theory has a detailed description of the two main types of visual capacity limitation. The limitation in storage capacity is incorporated through the *K* parameter, and the limitation in processing capacity is quantified by parameter *C*. Further, the question of early versus late selection is resolved in a novel way. In TVA, attentional selection and pattern recognition occurs *simultaneously* by encoding categorizations of objects into VSTM, and are thus conceived as two aspects of the same process rather than distinct processing stages (cf. Allport, 1993; Logan, 2002). The competitive aspect of attentional selection is modelled in terms of a parallel race between visual categorizations. Selection is based on pertinence values, which can represent both spatial and non-spatial properties. Whereas TVA is fundamentally an object-based model of attention, the CTVA extension of the theory accounts for many spatial effects (Logan, 1996). As one of the only models in the literature TVA incorporates Broadbent's distinction between stimulus and response set, in terms of pertinence and bias values, respectively. Finally, the efficiency of top-down control of attention is quantified by the relative attentional weights of targets versus distracters (parameter α).

Despite its broad scope TVA does not cover all major issues of visual attention. Notably, a concept of sustained attention is not currently incorporated (Peers, 2002). Parameter values are simply assumed to remain constant for the duration of the experiment. As noted in section 2.1, this is a weakness TVA shares with most other general theories of attention. In the context of the present dissertation, deficits in sustained attention can be regarded as a source of error rather than an object of direct interest. However, a possible way of checking for the influence of this factor is described in section 5.3, where it is suggested that variability in performance from trial to trial can be estimated using bootstrap statistics. Another major area not covered by TVA is the motor (e.g., orienting) aspects of visual attention. In tasks where stimuli are presented within a single fixation, such as the investigations of the present project, this factor can be neglected. Still, the interaction between motor processes and visual attention should be interesting for future developments of TVA. In relation to attentional control, TVA limits itself to describe how selection occurs once pertinence and bias parameters are set ("…placing a powerful mechanism at the disposal…of an intelligent agent"; Bundesen, 1990, p. 523). Thus the executive functions implied in parameter setting are not specified in TVA, but later extensions (ECTVA; Logan, 2001) have addressed this issue. In relation to the present experiments, it can be assumed that the experimental instruction plays the role of a homunculus, setting attentional priorities for the visual system (cf. van der Heijden, 2004).

Though TVA accounts for many findings and addresses most of the central issues in visual attention research, some of its basic assumptions are controversial. In particular, TVA is a parallel model of selection, and therefore challenged by the influential group of serial models (cf. section 2.2). Whether selection

generally works in a serial or parallel way is still unresolved (Kyllingsbæk, 2001), and to some extent the answer probably depends on the task. However, as argued in section 2.2, the parallel view appears to have gained much ground since the 1980s. In addition, TVA can in fact integrate serial mechanisms of attention. Bundesen (1990) accounted for findings in conjunction search by a "many-view" model, in which attention is shifted sequentially among subsets of items in the display so that processing is parallel within groups but serial between groups. The principle seems relevant to the more general question of eye movements and visual attention, but has not been much developed yet. Within the class of parallel models, there is controversy over another basic assumption of TVA. The biased competition theory holds that different categorizations of the same object tend to be mutually reinforcing, whereas categorizations of different objects inhibit each other's processing. Contrary, TVA assumes that categorizations are stochastically independent of each other. Strong independence has been shown under some circumstances (Bundesen et al., 2003; Nissen, 1985) but the general issue is still unresolved.

In summary, I have argued that TVA is a very strong model of visual attention, both in terms of theoretical scope and empirical precision. A few major theoretical issues fall outside the range of the model, and some of its basic assumptions are controversial, but it is hard to point to a part of visual attention research where TVA's account is clearly inferior to rival theories. For the purpose of the present dissertation it is particularly important that TVA's fits to whole and partial report data are unsurpassed, and that the parameters used to model these data also account for findings from a wide range of other attentional tasks. The latter fact is a strong

indication that the basic parameters of the TVA model, which are the focus of the patient testing, reflect central aspects of visual attention.

3. NEURAL THEORIES OF VISUAL ATTENTION

During the last decades cognitive research has increasingly been influenced by findings and models of neuroscience. The inspiration goes both ways. After all the brain is basically designed to carry out mental functions, and psychological theories are central to make sense of neural processes. The interaction between research areas has lead to the emergence of a new scientific field, cognitive neuroscience. Cognitive neuroscience draws on established disciplines such as clinical neuropsychology, cognitive psychology, neurophysiology, and statistics, and combines these elements for synergetic effects. The study of visual attention is arguably one of the most successful examples of this approach, mainly due to the fact that a solid theoretical basis was delivered from both psychology and neurophysiology. As described in the previous chapter cognitive research on visual attention has come a long way and, largely thanks to neurophysiological studies of primates, the functional anatomy of the visual system is among the best described in the brain (Desimone & Ungerleider, 1989; Zeki, 1993). Mappings of the visual system have revealed an intricate network of over 30 specialized cortical modules (Felleman & van Essen, 1991) and a generally accepted organizing principle has been found in Ungerleider and Mishkin's (1982) distinction between two cortical processing streams: A ventral occipito-temporal route for object recognition, and a dorsal occipito-parietal route for spatial cognition (or visuo-motor control; Milner & Goodale, 1995). Attentional modulation of the activity in the visual system has been described at macroscopic (section 3.1) as well as microscopic levels (section 3.2), providing converging evidence for neural theories of visual attention. In the following

some of the most important theories are reviewed to provide a background for understanding the effects of focal damage in the system.

3.1) Anatomical network models

The issue of anatomical localization of mental functions has always played a prominent role in neuropsychology. Historically the discussion has shifted from the extremes of phrenology (Gall & Spurzheim, 1808) and equipotentiality (Lashley, 1950) towards the contemporary emphasis on functional networks (Fuster, 2003). Today, complex mental activities are generally not viewed as the product of single centers (although tendencies towards "neo-phrenology" are still with us: see Uttal, 2001) nor of the brain in general. Rather, such functions are thought to depend on the integrated activity of large-scale networks, in which each component delivers a specific contribution. Research on this issue has been boosted enormously by the advent of functional neuroimaging, which enable in vivo measurements of the whole network during cognitive tasks. Inspired by these developments, as well as electrophysiological and lesion studies, several anatomical network models have been proposed for visual attention.

In line with the popular view in cognitive psychology that attention is inherently spatial, many models describe visual attention as controlled by spatial processing structures, typically located in frontal and parietal areas. A classic and still influential example of this type of model was presented by Mesulam (1981, 1990, 2000). Mesulam's network model includes three main anatomical nodes: the posterior parietal cortex, the frontal eye fields, and the cingulate gyrus. The parietal component, which is centered at the intraparietal sulcus, creates spatial maps of perceptual saliency and computes provisional plans for shifting (spatial) attention between significant

objects. The frontal component, centered at the frontal eye fields, converts these plans into specific motor sequences. The cingulate component influences object saliency by motivational and emotional factors. The three main centres are strongly connected to each other, as well as to supplementary areas in the striatum, pulvinar, and superior colliculus. The concerted activity of this network provides a "vector" function that determines the direction of attention in space. Functional imaging studies confirm that these structures are jointly activated in spatial attention tasks (Gitelman et al., 1999). There is a lateralization built into the model, such that the left hemisphere directs attention predominately to the right side of space, whereas the right hemisphere directs attention to both sides. This hypothesis is consistent with the notion that the perceptual style of the right hemisphere is relatively "global" versus a "local" bias of the left hemisphere (Robertson, Lamb, & Knight, 1988). Mesulam's hypothesis also provides a simple explanation for the marked lateralization of the neglect syndrome (see section 4.1), and several functional imaging studies have confirmed that the right hemisphere is more active in spatial attention tasks (Gitelman et al., 1999; Kim et al., 1999; Nobre et al., 1997). However the general evidence from functional imaging studies on this issue is mixed (Kastner & Ungerleider, 2000). Fink et al. (1997) reported largely symmetric activations under spatial shifts of attention, and others have reported more right-side activity regardless of the direction of attention (Vandenberghe et al., 1997). These varied findings suggest that the right hemisphere is dominant only for some aspects of spatial attention. One possibility is that voluntary (endogenous) shifts of spatial attention recruit activity bilaterally, but that the right hemisphere contains a specialized system for stimulus-driven (exogenous) reorienting of attention (Corbetta, Kincade, & Shulman, 2002).

Mesulam's model also includes a second main element, which is shared by most other theories. Independent of where attention is directed, a certain level of cortical arousal should be necessary for the attentional system to work (see also Heilman, 1979; Luria, 1973). The general level of arousal depends on the *ascending reticular activating system* (ARAS), which includes a number of brainstem nuclei (Moruzzi & Magoun, 1949) that project to widespread regions in the cortex by way of the intralaminar thalamic nuclei (see Heilman, Watson, & Valenstein, 2003). The ARAS system also has a biochemical component that involves multiple transmitter-specific pathways (Marocco & Davidson, 1998). Based on EEG and galvanic skin response studies of patients with unilateral brain damage, the right side of the brain seems most critical for bottom-up influences on arousal (Heilman et al., 2003). The activity of the ARAS system is also modulated top-down from limbic and frontal areas. These structures represent motivational and volitional factors necessary for sustaining attention in monotonous tasks (cf. section 2.1) that do not automatically engage the arousal system. As with the bottom-up component, Mesulam (2000) assumes that the top-down modulation of the ARAS system is lateralized to the right hemisphere. Both imaging and lesion studies confirm that the right prefrontal cortex and inferior parietal lobe are important for sustaining attention (Husain & Rorden, 2003; Robertson & Manly; 1999; Sturm et al., 1999).

Another highly influential model of spatial attention was proposed by Posner and Petersen (1990). This model includes three semi-independent networks that mediate different aspects of attention. The first is the posterior network, which is critical for orienting the (spatial) focus of attention. The posterior network is composed of the superior parietal lobe, the colliculus superior, and the pulvinar. These structures perform

the operations of disengaging, moving, and engaging (spatial) attention, respectively. This part of the theory is mainly based on spatial cueing studies of patients with selective lesions in one of the mentioned areas (Posner, Walker, Friedrich, & Rafal, 1984, 1987) who showed impairments in different parts of the cueing task depending on their lesion. Whereas the posterior network operates relatively automatically in response to external stimulation, the anterior network is responsible for executive control of attention and response preparation. This system was specified in less anatomical detail by Posner and Petersen, but the cingulate gyrus and the supplementary motor cortex were assumed to be central. Later studies of endogenous orienting of attention have instead pointed to the superior frontal lobe (Hopfinger, Buonocore, & Mangun, 2000), probably in close interaction with the intraparietal sulcus (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000). The third network in Posner and Petersen's model is responsible for general alertness. The network is assumed to depend mainly on the right hemisphere, and in general seems similar to the ARAS system described by Mesulam. Posner and Petersen's model is perhaps the clearest example of a supra-modal control system of attention. The activity in this system can be described as the *source* of attentional bias, which influences the activity of modality-specific *target* areas such as extrastriate cortex. The exact form of the response modulation in the target areas has been well characterized by single cell studies (see section 3.2), but neuroimaging studies have also consistently found that attention changes the activation of these areas (see Corbetta, 1998).

Particularly the notion of fronto-parietal control structures for attention has received strong support during the last decade (Giesbrecht & Mangun, 2002; Pessoa, Kastner, & Ungerleider, 2003). Combined frontal and parietal activations have

been found across a range of attentional tasks, including nonspatial ones, suggesting a general purpose system for attentional control (Wojciulik & Kanwisher, 1999). However other theories suggest functional subdivisions within the fronto-parietal system. For example it has been claimed that there are two fronto-parietal networks, specialized for endogenous and exogenous shifts of attention, respectively (Corbetta et al., 2002). The proposed system for endogenous shifts includes the superior frontal cortex and the intraparietal sulcus, whereas exogenous attentional shifting should depend on more inferior located areas in the right temporo-parietal junction and right inferior frontal gyrus. There is still no general agreement on these issues.

Many models have emphasized the spatial aspects of visual attention. However fronto-parietal systems may be equally important for nonspatial aspects of attention. For example, fronto-parietal areas are activated when paying attention to particular time intervals (Coull & Nobre, 1998), in relation to the attentional blink (Marois, Chun, & Gore, 2000), and during sustained attention (Sturm et al., 1999). A very recent line of investigations points to the importance of especially the parietal node for VSTM capacity (Owen, 2004; Todd & Marois, 2004; Vogel & Machizawa, 2004). Such general functions of the fronto-parietal networks fits with the biased competition theory of Desimone and Duncan (1995), which claims that attentional selection is the product of a distributed competition between object representations at many levels in the cortex, in which spatial properties have no special status. Thus there is no supra-modal system controlling the (spatial) focus of attention, but an interaction between many bottom-up and top-down influences on selection. A main source of top-down influences on attentional competition should derive from structures implicated in working memory, specifically the prefrontal cortex (Desimone, 1999). This top-down

bias can take many forms, and the non-specialized nature of prefrontal neurons has been emphasized in Duncan's (2001) *adaptive coding* theory, which claims that individual areas in the prefrontal cortex can adjust their function according to the requirements of the current task. Main support for this hypothesis, and for the biased competition theory in general, comes from single cell studies (see section 3.2).

In summary, the neural basis of visual attention is organized in large-scale anatomical networks. There is disagreement on the exact structure and functional organization of these networks, but some general features are widely accepted. A basic condition for attentional function is a sufficient amount of cortical arousal, and most theories relate this function to a cortico-subcortical system in which the brainstem, thalamus, and frontal/limbic structures are central (as well as transmitter-specific pathways). Both bottom-up and top-down regulation of this system seems to depend mainly on the right side of the brain. There is also wide consensus on the importance of fronto-parietal structures for control (or bias) of attentional selection. Neural models of visual attention typically include subcortical structures, especially the superior colliculus, the striatum, and the pulvinar nucleus, but the specific contribution of these areas is not clear. Corresponding to the variety of attentional functions described in cognitive psychology, these large cortico-subcortical networks seem to be involved in many different aspects of visual attention. However it is unclear to which extent the different functions are mediated by anatomically distinct circuits or general-purpose ("adaptive coding") networks. Further, although there is some evidence to suggest a special role for the right hemisphere, this issue is not settled. Influential theories hold that the right hemisphere is associated with bilateral ("global") visuo-spatial functions, but the evidence for this hypothesis is mixed. Perhaps the right hemisphere is

specialized only for stimulus-driven spatial shifts of attention. In general, the large cortico-subcortical networks modulate basic information processing in "target" areas located in the ventral and dorsal visual processing streams. The nature of this modulation is most clearly described in recordings of single cell activity, to which we now turn.

3.2) Visual attention at the single cell level

The action potentials (spikes) of individual neurons represent the basic level of information processing in the brain, and electrophysiological recordings of single cell activity provide a unique window to neural computation. The time interval between each spike of a given neuron varies considerably, but can be well approximated by the presence of a random Poisson process (Motter, 1998; Rieke, Warland, de Ruyter, van Steveninck, & Bialek, 1997). Each event (i.e., spike) in a Poisson process is stochastically independent from other events, and depends only on some constant probability per time unit. This implies that the information transferred between neurons is carried simply by the average firing rate rather than the specific time structure ("morse code") of the spike train. For that reason most models of single-cell information processing relate to the firing rate (e.g., Bundesen et al., in press; Reynolds, Chelazzi, & Desimone, 1999; Rieke et al., 1997) although response synchrony across neurons may also be important (Niebur & Koch, 1994).

One might expect that global psychological functions are not clearly reflected at this microscopic level, but the attentional state of the organism does in fact relate to firing rates in characteristic ways. Two decades of single cell research have revealed several distinct types of attentional effects in visually responsive neurons. One

common effect of visual attention is a modest modulation of the firing rate with a single stimulus in the receptive field (RF). The modulation can be negative (Motter, 1993) but typically firing rates are slightly increased (Connor, Preddie, Galant, & van Essen, 1997; McAdams & Maunsell, 1999a, 1999b, 2000; Motter, 1994a, 1994b; Reynolds, Pasternak, & Desimone, 2000; Treue & Martinez-Trujillo, 1999). These effects have been interpreted as a reflection of enhanced neural processing in the "spotlight of attention" (Connor et al., 1997) in line with influential cognitive theories (e.g., Posner, 1980). However, the findings can also be explained by a combination of feature-based attention (pigeonholing) and the influence of other (noise) stimuli than the one defined by the experimenter (Bundesen et al., in press). Besides, it should be noted that some studies have found no effect of attention with a single RF stimulus (Luck, Chelazzi, Hillyard, & Desimone, 1997; Moran & Desimone, 1985).

By far the largest effects on firing rates occur when several stimuli are present within the RF of the neuron. In this case attention to one of the objects modulates the firing rate up or down, depending on the cell's preference for the object. As remarked by Desimone and Ungerleider (1989) it seems as if the cell's RF contracts around the selected object (*dynamic remapping*). This filtering-like mechanism has been found for both spatial (Moran & Desimone, 1985; Reynolds et al., 1999) as well as non-spatial selection criteria (Chelazzi, Duncan, Miller, & Desimone, 1998; Chelazzi, Miller, Duncan, & Desimone, 2001). The fact that attention to (non-preferred) objects can dramatically *reduce* the cell's response is not consistent with the notion of response enhancement in an attentional spotlight. Instead these studies provide some of the most direct evidence for competitive, parallel processing mechanisms in attention (Desimone, 1999). Recall that in the biased competition theory of Desimone and Duncan (1995),

objects across the visual field initially activate many brain systems in parallel. Attentional selection is resolved by a competition between object representations that eventually leads to the domination of one object throughout. This model is strongly supported by recordings of V4 and IT neurons under visual search (Chelazzi et al., 1998, 2001). The response of the neurons was non-selective (i.e., equally determined by targets and distracters) for a period of about 200 ms. Then a dramatic change in response occurred so the cell's response was determined by the target object only. This happened even when the target stimulus was a non-preferred stimulus for the cell, such that attention effectively reduced the firing rate of the cell.

A third common effect of attention is an increase in the cell's baseline firing rate when a target is expected to appear in its RF (Chelazzi et al., 1998; Luck, Chelazzi, Hillyard, & Desimone, 1997; Miller, Erickson, & Desimone, 1996; Miller, Li, & Desimone, 1993; Reynolds et al., 1999, 2000). The baseline shift has been taken as evidence for top-down bias signals to the cell (Desimone, 1999) but can also be viewed as reflecting a mental image held in VSTM of the target stimulus (Bundesen et al., in press). The latter interpretation is supported by findings that similar attentional filtering occurs both with (Chelazzi et al., 1998) and without baseline shifts (Chelazzi et al., 2001).

The recently proposed neural interpretation of TVA (NTVA; Bundesen et al., in press) provided quantitative fits and detailed accounts of sixteen important studies in the single-cell visual attention literature. NTVA is the first model to attempt such general coverage of the field. The various findings were accounted for using the same basic principles as the cognitive TVA theory. In NTVA, the two selection mechanisms of TVA are interpreted as two orthogonal neural mechanisms. Filtering affects the

number of neurons that represent a particular object in their RF, whereas pigeonholing up- or downscales the activity in all cells coding for a particular feature. Following equation 1 of TVA, these two factors jointly determine the total activation of neurons representing a given categorization of an object. The total activation determines the speed at which the categorization is processed, and thereby its probability of being encoded into one of the few slots in VSTM. Bundesen et al. described hypothetical networks capable of carrying out these computations, and suggested a possible anatomical implementation in the brain. A central structure in the computational network is a *saliency map*, which determines the probability that individual cells contract their RF around particular objects. The saliency map was tentatively located in the pulvinar nucleus.

The attentional effects found in single-cell studies typically concern parts of the ventral stream of visual processing (V1, V2, V4, and IT), alternatively dorsal stream regions MT and MST, which can be viewed as lower-level "target" areas for attentional control. However single cell studies also provide evidence on the "source" of attentional bias signals. Prefrontal neurons can sustain object-specific signals over time, possibly representing a target template that biases attentional selection in visual areas (Desimone, 1999; Miller et al., 1996). In addition, neurons in a number of structures show activity related to general visual saliency: the frontal eye fields (Schall & Thompson, 1999), the lateral intraparietal area (Colby & Goldberg, 1999), and the pulvinar nucleus (Robinson & Cowie, 1997). Some theories (e.g., NTVA) claim the existence of a central saliency map, whereas others prefer a more distributed model of attentional weighting (Desimone & Duncan, 1995). In relation to brain damage, the former view predicts selective disturbances of attentional weighting after focal lesions

in the saliency map, whereas the latter view predicts mass-effects of brain injury (i.e, correlations between deficit and lesion volume, rather than location). However, since the activation in the saliency map should represent a summation of computations carried out in a wide range of cortical areas, mass-effects are also predicted in this case.

4. VISUAL ATTENTION DEFICITS AFTER BRAIN DAMAGE

Defined broadly, disturbances of attention are common after brain damage (Lezak, 1995). Research on attention deficits constitutes a large and heterogenous field, ranging from the effects of traumatic brain injury to developmental disorders, and no exhaustive review covering all types of brain damage will be attempted in this thesis (see van Zomeren & Brouwer, 1994). Instead the focus will be on visual attention deficits after unilateral stroke. These deficits can generally be categorized as lateralized and non-lateralized, a distinction that also represents the two main dimensions in the empirical work of the thesis. Classified under the syndromes of neglect and extinction, lateralized attention deficits have been much studied, and the relation to lesion anatomy is fairly well described (section 4.1). In contrast, non-lateralized attention deficits have typically been studied with less developed testing measures, often after diffuse brain damage, and clear relations to specific lesion sites are lacking (section 4.2). For both types of deficits I shall argue that important issues remain to be addressed (section 4.3).

4.1) Lateralized deficits in visual attention

By far the most studied disturbance of visual attention is the neglect syndrome, with hundreds of articles published over the last three decades. Neglect can be defined as a failure to report, respond, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion, when this failure cannot be attributed to either sensory or motor defects (Heilman, 1979). It is not hard to understand why research on this topic is popular. Neglect is a fascinating, paradoxical condition where patients are unaware of stimuli even though their perceptual apparatus is often intact. It is arguably one of the

clearest examples in neuropsychology of a selective disturbance of consciousness. In addition neglect is a frequent effect of stroke, especially in the acute stage, and therefore holds large clinical interest.

Early accounts described neglect as a sensory deficit (Battersby, Bender, & Pollack, 1956; Sprague, Chambers, & Stellar, 1961), but there are now strong reasons to regard the disturbance as primarily attentional. Hemianopia and neglect are doubly dissociable and related to damage in different parts of the brain (primary visual pathways vs. higher-level cortical areas, respectively; Heilman, Watson, & Valenstein, 2002). In addition, neglected stimuli can affect the patient's behaviour implicitly (Berti, 2002; Halligan & Marshall, 1988) indicating substantial cognitive processing beneath the conscious threshold. Neural correlates of this implicit processing have been found in the form of (relatively weak) cortical activations by the neglected stimuli (Rees, Wojciulik, Clarke, Husain, Frith, & Driver, 2000; Vallar, Sandroni, Rusconi, & Barbieri, 1991). Further, neglect is not necessarily retinotopic, but can be relative to different parts of the patient's body and even to the attended object itself (Rafal, 1998), which is not consistent with a simple sensory deficit. However a firm line between "lower-level" sensory and "higher-level" attentional processes cannot strictly be drawn, and the contemporary emphasis on attentional or "cognitive" explanations of neglect may have overshadowed basic sensory aspects of the condition (Halligan & Marshall, 2002). For example, under conditions where competing stimuli are absent and motor exploration is neutralized, perception of single contralesional flashes is deficient in neglect patients (Smania et al., 1998). The study of Habekost and Rostrup (2005a) suggests that similar sensory impairment can be found after many cases of right side brain damage, even when neglect is weak or absent.

Neglect is a complex disorder that involves many aspects of visuo-spatial cognition and behaviour (for an overview, see Karnath, Milner, & Vallar, 2002). It is now clear that there is no unitary neglect syndrome but rather a cluster of dissociable symptoms, where each patient is likely to display only a subset. Neglect typically affects perceptual function, but can also relate to motor function (Heilman et al., 2003) such that patients fail to respond to a stimulus even though they are aware of it. Though probably rare, studies have reported neglect confined to stimuli in near (reaching) space (Halligan & Marshall, 1991) and far space (Cowey, Small, & Ellis, 1994). Vertical neglect for stimuli in the lower (Butter, Evans, Kirsch, & Kewman, 1989) or upper visual field (Shelton, Bowers, & Heilman, 1990) has also been demonstrated. In general, lateral neglect tends to be stronger in the lower part of space (Halligan & Marshall, 1989; Pitzalis, Spinelli, & Zoccolotti, 1997). The visual aspect of neglect has dominated research, and is of course most relevant in the present context. However hemi-inattention is often manifest across sensory modalities and may include personal neglect, where one side of the body is neglected, and auditory neglect. Such generalized impairment is consistent with damage to supra-modal representations of personal and extra-personal space.

Although neglect also occurs after damage in the left side of the brain, evidence from thousands of patients shows that the condition is more frequent, severe, and persisting after right side damage (Mesulam, 2000). In particular neglect after left side injury seems to be rare beyond the acute stage (Stone, Patel, Greenwood, & Halligan, 1992). Several explanations have been offered for this marked lateralization. Mesulam (1981) suggested that the left hemisphere directs attention predominately to the right side of space, whereas the right hemisphere directs attention to both sides. This

way left side lesions should not cause much neglect because the right hemisphere can usually take over, whereas there is no similar “back-up” for the left visual field. The hypothesis of a bilateral attentional function of the right hemisphere was already discussed in chapter 3, where it was concluded that functional imaging evidence for the idea is mixed, and that the right side lateralization may be specific to stimulus-driven spatial shifts of attention.

In case of right side brain damage Mesulam’s theory predicts a sharp discontinuity at the vertical midline, dividing the visual field into an impaired and an (almost) preserved functional area. The *orientation bias* model of Kinsbourne (1993) presents an alternative to this view. Kinsbourne hypothesized that each hemisphere directs attention towards the opposite end of a visual display, but that these “opponent processors” keep each other in check by mutual inhibition across the corpus callosum. If the strength of one hemisphere is weakened by a lesion, the other hemisphere becomes hyperactive and pushes spatial attention in its preferred direction. Neglect’s relation to right side damage is explained by assuming that the left hemisphere processor is normally more powerful than the right hemisphere processor, and lesions of the latter therefore lead to more severe imbalance (Kinsbourne, 1987). Contrary to Mesulam (1981), Kinsbourne’s theory predicts a continuous gradient of performance across the visual field for neglect patients, peaking in the rightmost parts of space and worsening progressively as one moves leftward. However systematic mapping of the spatial attention of neglect patients (using reaction time to simple stimuli) has shown a clear-cut hemifield difference, with a local peak around 10 to 20 visual degrees within the right visual field (Marzi, Natale, & Anderson, 2002; Smania et al., 1998). Further, Kinsbourne’s notion of a hyperactive left hemisphere in neglect patients has not been

supported by physiological measurements, which instead point to reduced energy metabolism also in the intact hemisphere (Fiorelli, Blin, Bakchine, Laplane, & Baron, 1991; Perani, Vallar, Paulesu, Alberoni, & Fazio, 1993).

Another explanation for neglect's association with right side lesions relates to arousal and vigilance. Robertson (1993) noted that the frequency of neglect in the acute stage is quite similar after lesions in either side, but that only right side lesions lead to chronic deficits. Robertson proposed that two conditions are necessary for persisting neglect: damage to an orienting network and to a network for vigilance and arousal (cf. Posner & Petersen, 1990). Left side lesions affect only the orienting network, but due to the lateralization of the arousal system (cf. section 3.1), right side lesions lead to chronic disturbance in this system also. The early observations cited by Robertson of reduced arousal and vigilance in neglect patients have been confirmed, and in addition neglect has been associated with other non-lateralized disturbances of attention (Husain & Rorden, 2003; Robertson & Manly, 1999). These deficits include slow attentional blinks (Husain, Shapiro, Martin, & Kennard, 1997), reduced spatial working memory span (Wojciulik, Husain, Clarke, & Driver, 2001), and bilateral deficits in visual processing capacity (Duncan et al., 1999). Thus non-lateralized deficits have been established as an important part of the neglect syndrome, and represent a main explanation why some patients never learn to compensate for their hemi-inattention (Husain & Rorden, 2003). It is however unclear whether all the described non-lateralized deficits can be attributed to arousal disturbances. In particular, general reductions in VSTM capacity and visual processing speed may be related to damage in certain posterior cortical areas and their connections rather than the arousal system (see section 4.2).

Neglect is historically associated with parietal lesions (Brain, 1941; Critchley, 1949), later specified to the inferior parietal cortex (Vallar & Perani, 1986), which is still widely considered to be the main lesion location for neglect (Mort et al., 2003). Recently the traditional association with parietal lobe damage has been challenged by two large patient studies featuring new methods of lesion analysis (Karnath, Ferber, & Himmelbach, 2001; Karnath, Berger, Küker, & Rorden, 2004) that point to the superior temporal gyrus as the critical site. This issue is currently the focus of intense debate. However neglect has also been found after damage to other parts of the brain, though less frequently: the (inferior) frontal cortex (Heilman & Valenstein, 1972; Husain & Kennard, 1996), the basal ganglia (Damasio, Damasio, & Chiu, 1980; Karnath, Himmelbach, & Rorden, 2002), thalamus (Watson & Heilman, 1979), the cingulate gyrus (Watson, Heilman, Cauthen, & King, 1973), and internal capsule (Vallar & Perani, 1986). In addition, a large study by Samuelsson, Jensen, Ekholm, Naver and Blomstrand (1997) suggests that damage in the temporo-parietal white matter is necessary for the condition to become chronic. This diversity of relevant lesions makes sense if neglect is conceived as a "network syndrome" (Mesulam, 2000) where damage in multiple parts of an interconnected system for spatial orienting (and perhaps general arousal) lead to similar symptoms. It is currently unclear whether the different subtypes of neglect are related to damage in separate parts of this large-scale network. For example, it has been proposed that frontal lesions predominately lead to motor neglect (for a review, see Mesulam, 1999) or to increased distractibility for right side stimuli (Husain & Kennard, 1997). However other studies have not confirmed such functional segregations within the network (Mattingley, Husain, Rorden, Kennard, & Driver, 1998; see also Habekost & Bundesen, 2003). Simple mappings between

subtypes of neglect and particular brain areas are unlikely to be found if the anatomical network is so tightly knit that damage in individual nodes strongly affects other, structurally intact centres (by diaschisis) and if many of the component functions are distributed across several nodes. For example, parietal and frontal areas are both involved in perceptual and motor functions (Mesulam, 2002).

Neglect patients often show visual extinction, defined as a condition where contralesional stimuli are perceived normally when shown in isolation, but missed when accompanied by an ipsilesional stimulus (Bender, 1952). A strong attentional component in extinction is evident from demonstrations that performance can be improved by instructing patients to ignore ipsilesional events (Karnath, 1988), whereas sensory manipulations of the stimuli have minor effects (di Pellegrino & de Renzi, 1995). The definition of extinction implies a selective disturbance of attentional weights (i.e., an ipsilesional bias), whereas sensory effectiveness should be normal in both sides. However, as with neglect, there is now evidence that perception of isolated contralesional stimuli is often impaired in patients who show clinical extinction, though typically too slight to be detected in standard testing (Marzi, Girelli, Natale, & Miniussi, 2001).

Extinction is often considered to be a part of the neglect syndrome, or alternatively a milder form of neglect (Heilman et al., 2003; Kolb & Whishaw, 2003). However there are reasons to regard extinction as a separate entity. Double dissociations have been found between neglect and extinction (Cocchini, Cubelli, Della Sala, & Beschin, 1999) and the lesion anatomy of the two conditions are probably different, though overlapping (Karnath, Himmelbach, & Kuker, 2003). Specifically, extinction occurs after a wide range of unilateral lesions (Vallar et al., 1994) with simple lesion

volume as a major predictor (Habekost & Rostrup, 2005a; Peers et al., in press) and seems to be equally frequent after left and right side lesions (Peers et al., in press; Rafal, 1994). Besides being a common clinical phenomenon, extinction is interesting because it can be viewed as a prototype for (disturbed) attentional competition (Mattingley, 2002). This way the effect holds large interest for general theories of visual attention (e.g., the biased competition theory: Duncan, 1999). For example, extinction effects have been used to study interactions between grouping effects and attention (Ward, Goodrich, & Driver, 1994), and the saliency of face stimuli (Vuilleumier, 2000).

4.2) Deficits in the general capacity of visual attention

The theoretical distinction between energetic and structural limitations in attentional capacity (Cohen 1993; see section 2.1) is also useful for classifying general attentional deficits after brain injury. Energetic factors correspond to the neurological concepts of arousal and alertness. Alertness is often deficient in the early stages after brain injury, most severely in the acute confusional state where attentional functions are globally impaired (Mesulam, 2000). Acute confusion is typically caused by toxic-metabolic conditions and reflect disturbance in the subcortical arousal system (ARAS; cf. chapter 3). Given adequate treatment the confusional state usually wears off, but alertness can be disturbed after brain injury in other, more subtle ways. The activation of the ARAS system is top-down modulated by motivational and volitional factors, which primarily depend on limbic structures and the frontal cortex. Whereas subcortical disturbances of arousal lead to general reductions in attentional function, impaired top-down modulation typically leads to larger variability (attentional fluctuations), particularly when the external input is not engaging. Deficits in sustained attention seem related to

lesions in the right dorsolateral prefrontal cortex (Robertson & Manly, 1999), consistent with theories of the right hemisphere's involvement in arousal and vigilance (Heilman et al., 2003; Posner & Petersen, 1990).

If energetic factors can be assumed normal, the maximum processing ability of the individual depends on structural limitations in attentional capacity. Similar to cognitive psychology, clinical tradition distinguishes between two main types of deficit: reduced processing speed ("how fast?") and reduced span of attention ("how much?"). The first type of function is usually tested by reaction time tasks, whereas the second type is examined by tests of immediate memory span (Lezak, 1995). A tendency towards prolonged reaction time on cognitive tests has been found after nearly all types of brain injury (van Zomeren & Brouwer, 1987). The effect is traditionally considered a non-specific effect of brain injury, and research has focused on diffuse lesions such as head trauma or dementia (van Zomeren & Brouwer, 1994). Van Zomeren & Brouwer suggest that diffuse affection of the white matter (e.g., fiber shearing after traumatic brain injury) causes slower information transfer between brain centres (cf. Habekost & Rostrup, 2005b). However reaction time is a composite measure, and processing can be delayed at many stages between stimulus and response (Townsend & Ashby, 1983). Component analysis, where reaction times to various types of cognitive tests are compared, has been used to determine the locus of the slowness. For example it has been argued that traumatic brain injury leads to particular sluggishness in the decision making stage (van Zomeren & Brouwer, 1994), but such specific deficits have not been found in normal aging (Myerson, Hale, Wagstaff, Poon, & Smith, 1990) nor dementia (Cohen, 1993). In the present context the relevant variable is the speed of visual processing. Reaction time tasks are generally not adequate for measuring this function,

as the influence of motor processes and other factors is difficult to control for. Performance in attentional blink experiments should be more specific to the visual system. Husain et al. (1997) found a prolonged attentional blink in neglect patients, and recent results suggest that the deficit is related to damage in occipito-temporal and prefrontal cortex rather than neglect per se (Rizzo, Akutso, & Dawson, 2001). Perhaps the most specific measure of visual processing speed is obtained by TVA analysis of whole report data (see chapter 5). Using this technique, severe reductions in visual processing speed have been found in two cases of simultanagnosia (Duncan et al., 2003). There is also some evidence for the importance of the temporo-parietal junction (Habekost & Rostrup, 2005a; Peers et al., in press), but the data are still sparse.

Most neuropsychological tests of "attentional span" in fact measure auditory storage capacity (e.g., digit span, sentence repetition; for an overview see Lezak, 1995), and supposedly visual span tests such as Corsi Block Tapping rather examine the memory for sequences of movements. A valid test for VSTM capacity requires simultaneous presentation of items, so briefly that verbal recoding cannot influence performance. Change detection tasks have been used for estimating VSTM capacity in normal subjects (Luck & Vogel, 1997; Vogel et al., 2001), but the method has yet been little used in neuropsychological studies. Pigott and Milner (1994) used a variation of the paradigm, in which they tested the ability to detect changes in complex matrix patterns. Reduced performance was related to right frontal damage, but the very long exposure duration (2000 ms) and complex stimuli used probably invited strategic encoding, confounding the estimate of basic VSTM storage capacity. Other studies have used whole report experiments with a single exposure duration of such length (100 – 200 ms unmasked) that it could be assumed VSTM was filled up in each trial (Peers et

al., in press). However the most robust way of estimating the visual span limitation includes explicit control for the effect of visual processing speed. Whole report experiments with variable exposure durations (combined with TVA analysis, see chapter 5) currently seems to be only method for this. Few studies have been conducted using whole report tasks for measuring attentional capacity after brain injury, but evidence seems to be growing for the importance of posterior parietal areas (and their connectivity) for VSTM capacity (Habekost & Rostrup, 2005b).

Higher-level aspects of attention such as filtering, set switching, and monitoring can also be selectively disturbed after brain damage. The executive aspects of attention fall outside the scope of this thesis, but the basic filtering of visual distracters is directly relevant. As discussed in chapter 3, visual filtering probably depends on top-down signals from parietal and prefrontal (source) areas to (target) areas primarily located in the ventral visual stream. Accordingly, filtering deficits have been reported in a few cases of (bilateral) parietal lesions (Friedmann-Hill, Robertson, Desimone, & Ungerleider, 2003), prefrontal lesions (Gehring & Knight, 2002), and selective damage in visual area V4 (Gallant, Schoup, & Mazer, 2000). However TVA based investigations of visual filtering have been surprisingly negative (Duncan et al., 1999; Habekost & Bundesen, 2003) although some relation to lesion volume has been found in large patient groups (Habekost & Rostrup, 2005a; Peers et al., in press). These modest results are in line with the absence of findings after traumatic brain injury (despite subjective complaints; van Zomeren & Brouwer, 1994) and suggest that visual filtering is rather robust to brain damage. Alternatively, deficits in this function may require very sensitive testing to be demonstrated.

4.3) Limitations of previous studies

Numerous studies have been published on visual attention deficits, most of them related to neglect or extinction. Today these deficits are arguably among the best described in neuropsychology, and one might ask how the present project could contribute further to the field. Although previous research has greatly expanded our knowledge on lateralized attention deficits, I will argue that important questions remain to be answered. Also the field of non-lateralized attention deficits contains many unexplored issues. As will become clear from the following, the limitations of existing studies are mainly related to methodology.

Many lines of neuropsychological research originate in clinical observation of a single patient with abnormal behaviour. The investigation of such patients has been systematized in the case study approach, which provides in-depth analysis of a specific deficit pattern. Descriptions of single patients with inattention in selective parts of space (Butter et al., 1989; Cowey, Small, & Ellis, 1994; Halligan & Marshall, 1991; Kwon & Heilman, 1991; Rapcsak, Cimino, & Heilman, 1988, Shelton et al., 1990) have been central to the current understanding of neglect as a heterogonous syndrome. Also case studies of extinction patients have uncovered interesting cognitive and neural mechanisms (e.g., di Pellegrino & De Renzi, 1995; Rees et al., 2000; Rorden, Mattingley, Karnath, & Driver, 1997). In order to describe the patient's function in as much detail as possible, case studies use customized experiments that systematically test hypotheses about the nature of the impairment. Whereas this approach provides great precision in describing the patient's particular pattern of deficit, the general relevance of the tasks used is often unclear. In other words, the experiments are typically designed to characterize a very specific behavioural deficit rather than

relate to general theoretical constructs. This behaviourally driven, sometimes ad-hoc, approach makes it hard to compare results across patients, and especially renders the connection to theories of normal function difficult. Exceptions are found in the field of cognitive neuropsychology, which uses case studies of brain damaged patients to test general cognitive theories (Coltheart, 2003). However this line of research aims to elucidate normal cognition rather than clinical phenomena or brain-behaviour relationships. Accordingly, its influence on mainstream neuropsychology has been limited.

Although not strictly necessary to demonstrate reliable effects in a single person, most case studies describe patients with marked behavioural deficits. This way, case studies have a bias towards investigating strong functional impairment, and generally do not cover the full range of deficit severity after brain damage. Also in terms of mapping relationships between lesion location and deficit, case studies are not well suited for making general inferences. The importance of frontal (Heilman & Valenstein, 1972), basal ganglia (Damasio et al., 1980) and thalamic (Watson & Heilman, 1979) structures for visual neglect was initially suggested by observations of single patients. However stringent investigation of anatomy-function relationships requires studies of larger groups, including patients with similar lesions but no behavioural impairment. Case studies usually do not include control patients and tend to overestimate the effects of damage in a particular region, since the examined patient is selected specifically for having a deficit.

Investigating groups of patients is a logical follow-up to discoveries made in case studies. However the group study approach is faced with the difficulty that no two patients have exactly the same pattern of deficit. The customized testing that is used

in case studies must therefore be replaced by a general examination procedure, which inherently has lower specificity. More crude assessment is also rendered necessary by the fact that most group studies investigate patients in the acute stage of recovery, where large numbers of patients are still available in the hospital setting. Because fatigue is common in this phase, and complex assessment is generally impractical, tests must be easy to administer. Typically batteries of standard clinical tests are used (e.g., Farne et al., 2004; Karnath et al., 2001; Samuelsson et al., 1997). However these tests have relatively poor specificity, and for example cannot differentiate between the many subtypes of neglect demonstrated in case studies. Existing clinical tests are also inadequate to characterize the general capacity of visual attention, as argued in section 4.2. Besides specificity, the standard tests typically have lower sensitivity than the extensive, demanding tasks used for case studies or investigations of healthy subjects. For example, in their large study of extinction Vallar et al. (1994) compared the ability to detect unilateral versus bilateral finger movements (the clinical confrontation method). This type of stimulation should be well above threshold for many patients, and so milder attentional deficits were probably overlooked. Individualized testing with computer generated stimuli would have allowed stricter control of floor and ceiling effects (Mattingley, 2002). Thus, even though a broader spectrum of patients is examined than in case studies, group studies also tend to focus on marked clinical deficits.

This limitation aside, group studies are well suited to find general relations between lesion location and deficit. Early studies selected patients with a particular behavioural deficit (e.g., neglect symptoms on standard tests: Vallar & Perani, 1986; Husain & Kennard, 1996) and examined their lesion overlap. Recent studies have

recognized the need for including control patients without the deficit in question (Farne et al., 2004; Karnath et al., 2001, 2002, 2003, 2004; Mort et al., 2003). This makes it possible to perform subtraction analysis of lesions (cf. the thalamic patients in Habekost & Rostrup, 2005a), and gives more reliable estimates of the general prevalence of the deficit. For this purpose, patients are selected by anatomical criteria (e.g., right hemisphere damage) instead of behavioural symptoms. However, since patients are typically tested and scanned in the acute stage of recovery, diffuse affection of the brain (e.g., metabolic disturbances, diaschisis) is likely to complicate the lesion analysis, as well as confound the test results through general reductions of alertness. Also, investigations in the acute stage cannot inform about the eventual level of function, which is of large clinical interest. However inferences about anatomy-function relationships based on patients in the chronic stage are complicated by other factors. Over time patients may develop compensatory strategies, and intact tissue sometimes reorganizes and takes over some of the functions previously carried out by the damaged area (neural plasticity).

In summary, even though case and group studies of visual attention deficits tend to complement each other, it seems that important issues have not been covered adequately. Both types of investigation tend to focus on marked clinical deficits, which leave minor abnormalities relatively unexplored. This tendency is exacerbated by the fact that most large group studies have examined patients in the acute phase, where deficits are obviously more severe. The focus on symptoms in the acute stage also means that long-term effects of brain damage on visual attention are less well characterized. Another criticism that can be levelled against both types of design is that studies are typically driven by concepts derived from observations of

clinical behaviour rather than general cognitive theory. This incompatibility between the clinical neuropsychological and the cognitive psychological approach to visual attention makes it harder to answer the basic question of how normal cognitive function is changed by brain injury. A more integrated framework is also needed if lesion studies aim to contribute to the general mapping of functions in the healthy brain.

On the basis of these considerations there should be ample room for more studies on visual attention deficits, provided that methodology is improved on several points. To obtain a general picture of the effect of lesions in particular areas, patients should be selected by anatomical rather than behavioural criteria. This way selection is likely to include patients both with and without behavioural deficit, which allows localization of critical areas by subtraction analysis. In addition it seems useful to examine patients in the stable phase of recovery, where more extensive testing can be undertaken and lesion analysis is less confounded by general affection of the brain. Such investigations should also provide information on the important issue of long-term prognosis. Another central point is that testing should be grounded in general theories of attention in order to capitalize on the large set of theoretical developments and empirical findings in cognitive psychology. In chapter 5 such an assessment method based on the TVA theory is presented. In chapter 6, a series of studies are described that applied the TVA method in accordance with the other criteria outlined.

5. PATIENT ASSESSMENT BASED ON TVA

The TVA theory was developed in the context of cognitive psychology, and has been able to account for a wide range of findings on visual attention processes (cf. chapter 2). This success has recently motivated application of the theory in a different field of research: clinical neuropsychology. As argued in the preceding chapter, investigations of visual attention deficits should benefit from a stronger grounding in basic cognitive theory, and TVA seems to offer a powerful framework for such an approach. All the central parameters in the theory – visual threshold, visual processing speed, VSTM storage capacity, spatial bias, efficiency of top-down attentional control – should be clinically relevant, and can be accurately estimated from performance on two simple tasks (whole and partial report).

TVA based assessment depends on a specific combination of experimental testing and data analysis, the basics of which were established in a pioneer study by Duncan et al. (1999). The mathematical details of the data analysis were later generalized and implemented in computer software by S. Kyllingsbæk (www.psy.ku.dk/cvc). The investigations of the present project follow the general design laid out by Duncan et al., but elaborate the method on several points. A major development is the application of a novel way of estimating measurement error: bootstrap analysis (section 5.3). This chapter gives a general introduction to TVA based assessment and discusses theoretical and practical issues related to each component of the method. In particular, the possible problems of using a theory of normal function for brain damage research are considered. Besides the present project, the usefulness of the method can be evaluated from other recent studies that have used the TVA approach to

investigate brain damage. At the end of the chapter, the issues discussed lead to a general appraisal of the method.

5.1) Experimental designs: Whole and partial report

The main experimental paradigms used for patient assessment based on TVA are (visual) *whole report* and *partial report*. These are two classical methods for investigating divided and focused attention, respectively (Bundesen & Habekost, 2005; Neisser, 1967; Townsend & Ashby, 1983). Both paradigms have the virtue of a simple design. An array of simple visual objects is shown to the subject. The stimulation is typically so brief that eye movements are prohibited. In whole report, the task is to report the identity of as many items as possible. In partial report, only a subset of the stimuli defined by a selection criterion (e.g., a particular colour or location) is to be identified.

Whole report investigations date back to 19th century psychophysical research on the span of apprehension (Cattell, 1885; James, 1890/1950) and the method was reintroduced by Sperling (1960) in his famous studies on the available information in brief visual presentations. These and following studies confirmed Cattell's basic result from 1885: Normal observers can report a maximum of about four unrelated letters (*whole report limitation*). This result has proved to be fairly independent of variations in exposure duration and stimulus arrangement, and is traditionally interpreted as a reflection of the limited storage capacity of VSTM (Sperling, 1967). If the display is followed by a pattern mask, the mean score follows a characteristic function of the stimulus-onset asynchrony (SOA) between the stimulus array and the mask (the whole report function: Bundesen & Harms, 1999; Duncan et al., 1999;

Shibuya & Bundesen, 1988; present investigations). Below some minimum effective exposure duration (threshold) no letters can be reported without guessing. As the SOA exceeds the threshold, the mean score initially increases at a high rate, but then flattens out over the course of a few hundred milliseconds to approach an asymptotic value: the VSTM limit. The whole report function can be well characterized using three TVA parameters: The visual threshold t_0, the rate of encoding C, and the VSTM limit K (see section 2.2: Shibuya & Bundesen, 1988). When testing subjects with low visual processing speed, unmasked displays are sometimes used to prolong the effective exposure duration. The prolongation can be assumed constant across exposure durations (Bundesen, 1990) and is denoted μ. This parameter is useful for curve fitting, but has not received much independent interest.

Whole report can be viewed as a special case of partial report in which the number of distracters is zero (i.e., all items are targets). In partial report proper, targets are shown intermixed with distracter items. Targets are distinguished from distracters by a selection criterion (e.g., a particular colour, location, or alphanumeric identity). In TVA based assessment the selection criterion is given in advance of the display, but in the partial report experiments by Sperling (1960) the subject was informed of the selection criterion (i.e., a particular location given by an auditory cue) after the display had vanished. Sperling found that for displays with many items, the percentage of targets correctly reported was strongly increased by changing the instruction to partial report (*partial report superiority*). Partial report superiority is also the rule in experiments where the selection criterion is known in advance: Accuracy for a given target generally declines more by adding another target than a distracter item to the display, an effect that has been found for many different selection criteria (Bundesen et

al., 1984, 1985; Shibuya & Bundesen, 1988; Duncan, 1980; Shibuya, 1993). The efficiency of selection varies widely with the choice criterion. For example, selection by colour can be nearly perfect (Harms & Bundesen, 1983) whereas selection by alphanumeric identity is much harder (Bundesen et al., 1984, 1985). The different effects on performance by target and distracter items are quantified by the parameter α in TVA (cf. chapter 2: equation 3). As in whole report, partial report stimuli can be followed by a pattern mask (Habekost & Bundesen, 2003) or shown unmasked (Habekost & Rostrup, 2005a, 2005b). Masking the stimuli enables testing near the perception threshold, which may increase the sensitivity of the test. Use of unmasked stimuli has the advantage that colour-based selection is not disturbed by the mask, and perception of multiple items can be tested due to the longer effective exposure time.

Detailed mathematical models of whole and partial report performance were developed in the 1980s (Townsend & Ashby, 1983; Bundesen et al., 1984), culminating in the very close fits provided by the FIRM model (Shibuya & Bundesen, 1988). By being a generalization of the FIRM model in a strict mathematical sense, TVA inherits this success. According to FIRM/TVA, whole report performance depends on the values of three parameters: t_0, C, and K, and partial report data can be described by invoking two additional parameters: w_{index} and α. Since all the main parameters in the TVA model are reflected in whole and partial report data, the paradigms seem to offer a simple yet powerful tool for measuring general aspects of visual attention. Still, various aspects of the paradigms' validity have to be considered.

In experimental psychology cognitive processes are investigated through abstraction of the (supposedly) defining characteristics of real life activities in order to study these in pure form in the laboratory. One example of this approach is investigation

of visual attention through the lens of whole and partial report paradigms. Strictly speaking these experiments do not measure high-level constructs such as visual processing speed or top-down selectivity, but rather the ability to report unrelated letters presented within a single fixation. It is not immediately obvious how performance on such tasks is related to visual attention in general. Main support for the validity of the approach comes from the fact that the TVA parameters used to model the data can also account for a wide range of findings from other experimental tasks (cf. chapter 2). However the validity of a psychological test potentially has many sides depending on which inferences are drawn from it. Besides the relation to other experimental studies, four relevant aspects of the paradigms' validity are: (a) the relation of the particular stimulus material to visual objects in general, (b) the relation to perception that involves more than a single fixation (i.e., exploratory activity), (c) the relation to other clinical measures of visual attention, and (d) the functional specificity of each TVA parameter. Each of these issues will be discussed in turn.

In TVA based assessment the usual stimulus material is single letters. There are several reasons for this choice. Letter perception is a precondition for one of our most important visual activities: reading, and as such an interesting object of study in itself. More importantly, letters seem well suited for investigating perception of (simple) visual objects in general. Letters are perhaps the most over-learned visual forms in our environment, and recognition is highly efficient. This means that VSTM can be filled up within a few hundred ms (i.e., a single fixation), which is practical for assessing the limits of this function. In addition, letters are elementary visual forms in the sense that they can be processed in parallel (Kyllingsbæk, Schneider, & Bundesen, 2001) and probably have a structural complexity corresponding to the response tuning

of individual IT neurons (Tanaka, 1993). TVA based assessment mainly targets high-level attentional mechanisms, and it would be a confounding factor if the basic recognition of the test stimuli was deficient. Therefore it is practical that letter perception is quite robust to brain damage, especially if the left side of the brain is not affected. Another practical property is that the alphabet is so large that many different letters can be presented in the same display without risk of having the score confounded by guessing. Also, the individual items are approximately equally difficult to identify (the stimulus set is homogenous), which simplifies the data analysis. In addition, response (i.e., verbal report) is straightforward. For all these reasons, letter stimuli have been widely used in previous research. This allows results to be easily compared with many other studies, but on the other hand the empirical basis for generalizing to different stimulus types is rather weak. In summary, as a means to probe the general efficiency of visual attention processes it seems that letter stimuli have many practical advantages. It is reasonable to assume that letters are representative of simple visual objects in general, but caution should still be applied when generalizing results to other stimulus types (e.g., faces).

The presentation of stimuli in whole and partial report is *tachistoscopic* in the sense that it is limited to fractions of a second. Although this situation may seem artificial, it is in fact an extremely general visual phenomenon. In our normal visual activities, from reading to perceiving a scene, perception of the surrounding environment is built up through an ongoing cycle of saccades and fixations (Gibson, 1979). This is due to the highly uneven distribution of acuity in the visual field, which makes foveal vision necessary for detailed object recognition. Between each saccade the eyes remain relatively still (apart from micro-tremor, nystagmus, and drift) for about

200 - 300 ms, during which visual information is collected. Information uptake is inhibited during saccades, which in effect makes the eye a tachistoscope (Rayner, 1998). Thus, the processes measured in whole and partial report experiments can be said to reflect the most basic building block in the visual process: The information uptake of a single fixation. However in terms of TVA it is unclear how this ability relates to perception in general, that is, constructed over multiple fixations. Especially in relation to brain damage, the question of compensation for (or worsening of) visual deficits through orienting behaviour is interesting. Some indication of the interaction between perceptual and motor factors can be deduced from comparing TVA estimates with performance on standard neglect tests (which allow explorative eye movements) and reports of daily life function, but more principled experimental research is needed. Still, it seems highly plausible that a visual abnormality evident in single fixations should also affect perception in general.

In the absence of a "gold standard" against which visual attention tasks can be measured (criterion validity), validity depends on the gradual development of converging evidence from related, but non-overlapping measures (construct validity). In the case of whole and partial report this process is only beginning. The first systematic attempt to compare TVA based assessment with clinical attention tests was recently carried out by Finke et al. (submitted; quoted with permission). In addition to TVA based assessment, 38 healthy participants were given various standard clinical tests, each of which were selected to correspond (roughly) to a specific TVA parameter (i.e., C: a test of phasic alertness; K: a test of visual memory span; w_{index}: a lateralized visual scanning task; α: a version of the Stroop test). Significant correlations were found between all four TVA parameters and their paired clinical test. Equally important, the

TVA parameters generally did not correlate with their non-paired tests (apart from *K* values and visual scanning). Although the TVA parameters do not represent exactly the same functions as the selected clinical tests, the specific correspondences are encouraging.

In principle the various TVA parameters represent separate aspects of visual processing, and the model does not specify any dependence between their settings. However in reality, it is conceivable that the different parameters depend on the same abilities to some extent, which would lead to correlations in their values. Finke et al. also examined this issue of *discriminant validity,* and computed correlations between the values of all four TVA parameters. Only *K* and *C* were significantly correlated (to a moderate degree: $r = 0.40$). In a smaller control group of twelve subjects tested by Habekost & Rostrup (2005a, 2005b) there was a similar tendency for *K* and *C* values to be moderately correlated. Besides the possibility that individuals vary in a general level of visual capacity that is reflected in both processing speed and VSTM capacity, the *K* - *C* correlation may be an artefact of the data fitting procedure. There are substantial analytic problems with extracting separate measures of *K* and *C* from a limited number of data, which are discussed in section 5.2.

To interpret whole and partial report performance solely in terms of TVA parameters it must be assumed that other, necessary components of performance can be neglected (i.e., are normal). A basic condition is that visual field cuts must be absent. If the patient has field cuts, *C* values are reduced to zero at certain display locations, which makes testing pointless. Visual processing is not measured directly, but through verbal report. Therefore visual-to-verbal recoding should be adequate, and expressive aphasia must be absent. Also visual acuity must be sufficient (i.e., not cause special

difficulties for discriminating letters, or distinguishing targets and distracters. The latter operation depends on colour acuity in the present studies). Participants should be highly trained in recognition of letters (i.e., literate and with an intact letter recognition system in the brain, usually located in the left hemisphere). Verbal storage capacity must be larger than VSTM capacity in order not to confound estimates of the latter. Further, arousal levels must not be significantly reduced, and participants should be able to understand the instruction. In studies of normal cognition, where young university students comprise the usual study population, all these factors can be taken more or less for granted. However in brain damage studies, screening and control procedures must be included to ensure that performance is not confounded by some of these deficits. Motor activity is another process that is not modelled by TVA. To eliminate the influence of this factor, report must be unspeeded and stimulation so brief that eye movements are not possible during the presentation (i.e., $\leq$ 200 ms). Central fixation can be controlled by direct observation (Duncan et al., 1999; Habekost & Bundesen, 2003), video recordings (Habekost & Rostrup, 2005a, 2005b) or special equipment for detection of eye movements (Peers et al., in press).

The design of the experiments should also control for other possible confounds. For example, visual inattention may increase with eccentricity from the vertical midline (Smania et al., 1998). To hold this factor constant between items, stimuli can be presented in a vertical column (Habekost & Bundesen, 2003). However to simplify modelling it is also useful if visual acuity is equal across display positions. This can be approximated by presenting stimuli at the same visual angle from fixation (i.e., at the circumference of an imaginary circle centered at fixation: Habekost & Rostrup, 2005a, 2005b). It also simplifies the interpretation of results if there are no

systematic differences between how individual subjects allocate their attention voluntarily. Therefore, participants should be encouraged not to allocate attention covertly to other locations than a central fixation point before stimulation. Besides explicit instructions, an effective way to achieve this is to randomize the spatial presentation from trial to trial. Another point concerns individual differences in response bias. If different participants adopt either very conservative or very liberal criteria for reporting items, their scores will not be directly comparable. The error rate is an objective measure for the participant's guessing bias, and can be controlled at an approximately fixed level (e.g., 10%) by continuously giving feedback on performance and asking participants to adjust their reporting accordingly. An alternative method is to use forced choice reporting and correct the score for guessing.

5.2) Data modelling: Parameter estimation

Whole and partial report experiments provide a large set of observations for each participant (e.g., 1120 different trials in Habekost & Bundesen, 2003). Given a psychometric model (e.g., TVA) of the general probability distributions underlying these observations, the unknown parameters of the distributions can be inferred. The standard mathematical procedure for this estimation is the maximum likelihood method (Morgan, 2000). Basically this is a computational algorithm that searches parameter space for the set of values that maximizes the probability of obtaining the actual set of observations. Customized software for maximum likelihood estimation of TVA parameters from whole and partial report data has been developed by S. Kyllingsbæk (www.psy.ku.dk/cvc/tva). However before this automatic procedure is set to work, non-trivial decisions must be made on the model used to fit the data.

The combination of whole and partial report data allow all the basic TVA parameters (t_0, C, K, α, and w_{index}) to be inferred. If the experiments include lateralized presentations, four of these parameters can be estimated separately in the left and right visual fields (the fifth parameter, w_{index}, by definition relates to bilateral stimulation). In principle, individual values for each display position can even be estimated for most parameters. However before attempting to determine all these parameters from the data the problem of *over-fitting* must be considered (Morgan, 2000). Performance on all experimental conditions (unless they are at floor or ceiling) varies from trial to trial. This is a simple empirical fact, but also consistent with TVA's assumption about the stochastic nature of visual recognition. From a model fitting perspective this variability introduces noise in the data set. A fundamental question for the data analysis is how many, and which, parameters can be inferred reliably from a limited set of noisy observations.

Earlier studies that established the ability of TVA (and the predecessors of the model) to fit whole and partial report data used large numbers of trials to estimate only a few parameters. In the study of Bundesen et al. (1984) each participant completed 1440 trials in Experiment 1, and 1080 trials in Experiment 2. Three parameters (K, α, and a noise parameter "ε") were estimated from the data. In Shibuya and Bundesen (1988) four parameters were estimated (t_0, C, K, α) using an impressive 6480 trials for each participant. Bundesen and Harms (1999) estimated just two parameters: t_0 and v, but nevertheless used 20 levels of exposure duration and 200 trials per condition, adding up to 4000 trials per participant. Such thorough investigations produce very reliable parameter estimates for each participant. However when testing brain damaged patients the number of trials often has to be limited for practical reasons,

such as fatigue and the transportion costs related to multiple testing sessions. For example Habekost and Bundesen (2003) used 480 whole report trials and 640 partial report trials, and Habekost and Rostrup (2005a, 2005b) used 300 whole report trials and 300 partial report trials.

Besides a less than optimal number of trials, the study population in itself can present difficulties. Whereas participants in previous TVA studies were young, the subjects in the study by Habekost and Rostrup (2005a, 2005b) averaged about 55 years and a majority had brain damage. Presumably because of this, encoding speed was generally reduced compared to earlier TVA studies, especially in the contralesional side. Therefore the VSTM limit was typically approached rather slowly, and some participants only reached their maximum score a few times on the longest exposure durations. Weaker constraint from the VSTM limit makes it harder to pin down the different contributions of *C* and *K* to performance at intermediate and long exposures. In earlier TVA studies this analysis was straightforward due to an initial sharp rise in the whole report function, which could be attributed to *C,* followed by a long, flat increase towards the asymptote, reflecting *K*. However in the investigations of Habekost and Rostrup (2005a, 2005b) many patients had just a few scores at their maximum level, and often obtained this score only in the ipsilesional field. The analytic problem was alleviated by estimating the *K* parameter across both visual fields so that the estimate was based on the double number of trials, including performance in the "strong" ipsilesional side. There are both empirical and theoretical reasons to regard VSTM capacity as a general (i.e., bilateral) limitation. In Duncan et al.'s (1999) TVA study of neglect patients scores were generally high, and *C* - *K* differentiation can therefore be assumed reliable. Duncan et al. found no difference between *K* in the left

and right visual fields, even in neglect patients with clear reductions of processing speed in the left side. The control subjects also had *K* values that were close to symmetrical. Besides this empirical finding there are theoretical reasons to assume lateralized differences in processing speed, but not in VSTM capacity. VSTM is conceived as the end-point of visual processing, a central limitation in the cognitive system, whereas *C* reflects the total processing capacity across the visual system. Visual processing is known to be lateralized to a high degree, so it is plausible that its efficiency can be damaged unilaterally. In contrast, VSTM capacity probably depends on a more centrally localized system. Whole and partial report experiments require letter identification, and it can be assumed that stimuli do not reach VSTM until processing involves the left hemisphere (cf. hemi-alexia after callosal lesions; Molko et al., 2002). To summarize, both a limited number of experimental trials and a generally low performance level in brain damaged populations call for a robust parametrization, which focuses the investigation on as few parameters as possible. The exact choice of model should be based on theoretically plausible assumptions weighed against the main interest of the investigation (e.g., left-right comparisons).

In addition to restraining the number of parameters in the model, it is useful to set a priori limits for estimates. Some parameter estimates depend on experimental conditions in which data are sparse, which can lead to fits that are clearly implausible. For example if the slope of the whole report function is shallow (so that the function does not seem to rise sharply form a well-defined point), t_0 estimation can be unreliable and in some cases drop to 0 ms. However it is highly implausible that post-masked letters displayed for only a few ms can be reported, as implied by such low t_0 values. Based on thorough studies of young healthy subjects (Bundesen & Harms, 1999;

Shibuya & Bundesen, 1988) a minimum limit of 15 ms seems reasonable. Also an individual limit for *K* can be set to prevent the estimate from going higher than the best score obtained by the participant.

If partial report is conducted with one fixed exposure duration for each participant, the influence of sensory effectiveness and VSTM limitation cannot strictly be distinguished. However a rough approximation of VSTM capacity, *K'*, can be obtained from the raw data, and used as a *plug-in estimate* in the modelling of other parameters. *K'* is given by the frequency-weighted average of the highest and next-highest score obtained by the participant (Peers et al., in press). The approximation assumes that exposure duration is so long that VSTM is always filled up, and that performance is thus exclusively limited by VSTM capacity. In most cases this is a simplification, but since VSTM capacity is often of secondary interest in partial report experiments, this is a minor source of error. For example, a less reliable *K'* estimate should not disturb the estimation of side differences in attentional weights.

Another problem for model fitting occurs if a participant obtains only a few scores at her/his performance maximum. The question is whether such observations should be considered valid or discarded as outliers. If discarded, it is not clear whether the cut-off point should be set at one, two, three, or perhaps four of such "outlying" observations. The precise value of this criterion is arbitrary, but can have large consequences for the analysis. Especially estimation of *K* depends heavily on the highest scores in the data set. It is not obvious why an observation should be considered invalid just because it occurs rarely. Exclusion of data can be justified if the observations are caused by guessing, such that a participant with, say, a maximum VSTM capacity of three elements occasionally reports four items by guessing the fourth

letter in the display. However under most circumstances this is not likely. For example, with 17 letters in the stimulus set (Habekost & Rostrup, 2005a, 2005b) the probability of guessing one of the remaining two letters in the display after having recognized three others is: $p = 2 * (1 / (17 – 3)) = 0.14$. If VSTM capacity is four at maximum, the probability of guessing the fifth letter is even lower: $p = 1 / (17 – 4) = 0.08$. The problem is also minimized by explicitly instructing participants not to guess, but only to report letters they are fairly certain of having seen. In the present investigations participants with "outlying" scores typically made only one or two reports above their usual reporting maximum. Thus it is unlikely that the highest score was due to guessing, especially if the score occurred more than once. The simplest solution to the outlier problem seems to be to treat all observations as valid unless special circumstances (e.g., many reports in a given condition but only a few correct, implying a guessing strategy) are evident.

5.3) Bootstrap analysis: reliability of estimates

As discussed in section 5.1, validity is central to the quality of empirical measurements. However the *reliability* of measurements is just as critical. It is logically impossible to demonstrate validity in a measure with zero reliability, and in general the reliability of a test constrains its maximum level of validity (Kaplan & Sacuzzo, 1997). Reliability refers to the consistency of a person's scores on a series of measurements (Cronbach, 1959). Standard test theory assumes that the observed score is a sum of the person's "true score" and some measurement error (in TVA based assessment, the measurement error includes the "true" variability inherent in the visual recognition process). Errors of measurement are assumed to be random, and the true score is thus the expected average

value obtained from an infinite number of test administrations (assuming no practice effects or other changes in the person's true ability). Of course in reality, the person's true ability has to be estimated from a limited number of observations, which means that measurement error may influence the estimation significantly. The relative magnitude of measurement error determines the reliability of a test. A standard way of estimating reliability is by repeated administrations of the test with a large group of subjects, in order to compute the correlation between performance on the first and second administration (test-retest reliability). Test-retest investigations have so far not been carried out for TVA based assessments. A practical obstacle is that a standard set of whole and partial report experiments takes several hours to complete, which makes a second round of testing quite time consuming. More principally, test-retest studies are subject to changes in true ability (e.g., practice effects), which is a different phenomenon than the reliability (precision) of the test itself. Also, performance may not vary to the same extent for different individuals. By being based on the average difference between two assessments in a group of control subjects, test-retest correlations do not directly concern the measurement error of a particular subject's test results.

With the aid of modern statistics, one can estimate an aspect of reliability that relates uniquely to each test administration. Unlike test-retest reliability, this aspect corresponds to what might be called test-internal consistency of performance. Given a set of observations from a particular test session, it is relevant to know how much confidence can be put in one's estimate (θ') of the real parameter value (θ) supposed to underlie performance. In other words, in addition to parameter estimates one needs an estimate of the measurement error related to the parameters (Wichmann & Hill, 2001).

A powerful method to do this is provided by bootstrap analysis, which was introduced by Efron (1979). The bootstrap method has been the subject of much statistical research (Chernick, 1999; Efron & Tibshirani, 1993) but the basic idea is simple. The bootstrap method is a Monte Carlo *resampling* procedure that generates a set of synthetic data (the *bootstrap sample*) based on the original set of observations. The resampling is done randomly and independently (Monte Carlo sampling) until the bootstrap sample contains as many "observations" as the original sample. The resampling is done with replacement, so a given original observation can be included more than once in the bootstrap sample, or may not be included at all. This way each bootstrap sample represents a systematic variation of the original data, and parameter estimates (θ^* values) computed from these data varies from one bootstrap sample to the next. The key idea of the bootstrap is that the variation between parameter estimates based on bootstrap samples (θ^* values) can be taken as an approximation of the measurement error inherent in the parameter estimate (θ') of the original data. Specifically, it can be shown that the variability of θ^* around θ' converges to the variability of θ' around θ (i.e., the true measurement error) given reasonably general assumptions (Chernick, 1999). The most central of these assumptions is the *bootstrap bridging principle*: That the original parameter estimate θ' is "close enough" to the true value θ for the variability around the two values to be similar (Wichmann & Hill, 2001). The validity of the bridging assumption depends on the smoothness of the estimator function (which is well-behaved in case of TVA analysis) and the quality of the original sampling procedure. For a psychological experiment, this implies a sufficient number of trials and an efficient sampling scheme for the investigated effect (e.g., a broad selection of

exposure durations to sample the main aspects of the whole report function). All these conditions seem to be satisfied for TVA based assessment.

The main application of the bootstrap method, and the one used in TVA based assessment, is approximation of the standard error of a given parameter estimator. The standard error can be used for construction of confidence intervals for the estimator, given that the estimators are normally distributed. In this case, 95% of the bootstrap estimates lie within plus/minus 1.96 standard errors of the mean (cf. Habekost & Rostrup, 2005a). This is equivalent to stating that the estimated parameter value is significantly different (at $p < 0.05$) from values outside the confidence interval. The sufficient number of bootstrap samples for this analysis is controversial, and because of the computational complexity of estimating TVA parameter values the issue is not trivial: 1000 bootstrap repetitions takes many hours to compute even on a PC running at 2-3 GHz. Efron (1987) originally proposed that 100 repetitions were sufficient for estimating the standard error of measurement, but this has been challenged (Chernick, 1999). In case of confidence intervals more repetitions are required because there are relatively few observations at the tails of the distribution (i.e., the extreme 5%) that determine the boundaries of the confidence interval. Efron (1987) suggested that 1000 repetitions are sufficient. However the 1000 repetitions is only a rule of thumb and the issue also depends on the data material, particularly the number of original observations. Informal tests suggest that TVA based estimation reaches asymptote after much less than 1000 repetitions (unpublished data), probably due to the many observations in each data set.

Bootstrap analysis generally shows that TVA parameters and the indices derived from them are very reliable (Habekost & Bundesen, 2003; Habekost & Rostrup,

2005a). Especially *K* seems to be strongly constrained by the data, with a typical measurement error of less than 5% of the actual estimate. The generally high reliability should increase the power of TVA based assessment to find significant effects, which is probably the main reason why small deficits in individual patients have been detected so consistently. For example Habekost and Rostrup (2005a) could demonstrate significant asymmetry of visual processing speed in 13 out 14 patients with large lesions, although the deficits were generally minor. There is however one exception to this rule: Estimates of the α parameter are systematically less reliable. This could reflect special difficulties at sustaining a stable level of visual filtering throughout the experiment, but the measurement error is also evident in simulated data (Kyllingsbæk & Habekost, unpublished data). These simulated data were produced by setting up a (digital) "perfect TVA observer", which is programmed to "score" exactly according to a particular set of parameter values (e.g., $K = 3.5$, $C = 20\ s^{-1}$, $\alpha = 0.5$ etc.) combined with the exponentially distributed variability inherent in the recognition process. Such an observer is of course not affected by energetic fluctuations in attentional function, but still α estimates showed much larger measurement error than other parameters. The effect may be explained by the fact that α is defined as a ratio of parameters, which should make it vulnerable to random variations in both the denominator and numerator. However more investigations are necessary for a full explanation.

Bootstrap analysis has been applied in many areas of science (Chernick, 1999) including psychophysics (Maloney, 1990; Wichmann & Hill, 2001), but prior to Habekost and Bundesen (2003) the method has not been used in the context of neuropsychological assessment. However bootstrapping offers several advantages for examination of cognitive deficits, especially at single case level. By computing

confidence intervals for each test result, it can be tested whether a given patient's score deviates significantly from some criterion value (e.g., $w_{index} = 0.50$, representing symmetrical attentional weighting; cf. Habekost & Rostrup, 2005a). Significance testing can thus be applied at the intra-individual level. In general, knowing the measurement error of a given score provides extra information to guide the interpretation. For example, prior to the introduction of bootstrap analysis it was not known that α estimates are less reliable than the other TVA estimates. However it is now clear that single abnormal values of this parameter should be interpreted with caution, or conversely, that absence of findings on α may reflect low statistical power (Habekost & Rostrup, 2005a). Another useful feature of bootstrap analysis is that it can alert one to abnormalities in the data sampling of a particular patient. For example, the w_{index} value of a particular patient tested by Habekost and Rostrup (2005a) had an unusually large standard error, which turned out to reflect a problem with ceiling performance in one of the conditions in the experiment.

A final application of the bootstrap method should be mentioned, though it has not been systematically explored yet. Relatively large bootstrap standard errors in an individual participant's TVA estimates may be taken as an indication that performance fluctuated more than usual during testing (i.e., attention was poorly sustained). If for example the "true" C values of the individual fluctuate between 10 s^{-1} and 20 s^{-1} during the experiment (compared to being stable at 15 s^{-1}) performance from trial to trial should vary more, leading to a relatively large standard error of the person's C estimates. In the group study by Habekost and Rostrup (2005a, 2005b), the relative measurement error on parameters C_{left} and C_{right} was slightly higher for patients with large lesions compared to control subjects (10% vs. 7 – 8%). The difference was

statistically significant. There were no corresponding differences in relation to parameters K and w_{index}. It is not clear whether the slightly less reliable C estimates of the patients were due to disturbances of sustained attention or analytic difficulties related to estimation of low processing speeds. Further investigations, including simulated data, should clarify whether the bootstrap method is useful for detecting abnormalities of sustained attention.

5.4) Other studies featuring TVA based assessment

The TVA approach to brain damage assessment was introduced only about five years ago. Yet, a number of studies have already been conducted prior to or in parallel with the present project. The method was originally presented by Duncan et al. (1999), who studied nine patients with neglect. Besides establishing TVA based patient assessment, Duncan et al. found a range of interesting results. As expected, the neglect patients had low attentional weighting of contralesional objects. However no deficit in top-down selectivity could be demonstrated in either field, whereas the storage capacity of visual short-term memory was reduced bilaterally. Visual processing speed was also reduced in both hemifields, though more in the left side. The mixture of preserved, unilaterally deficient, and bilaterally deficient functions was a strong demonstration of the specificity of TVA based assessment, and went beyond simple notions of neglect as a general contralesional deficit. The same experimental design (whole report only) was used in a case study of a patient with selective problems in visual shape integration (Gerlach, Marstrand, Habekost, & Gade, in press). The investigation showed that the patient's visual capacity was intact in most respects, but unlike control subjects her attentional resources were focused at a single rather than multiple locations in the

display (local bias). The case study approach was also used by Duncan et al. (2003), who tested two patients with simultanagnosia by whole report. It is traditionally assumed that patients with this disturbance can only process a single object at a time (i.e., $K = 1$), but Duncan et al. showed that the two patients were in fact able to recognize up to three objects simultaneously. However their perception was characterized by extremely low visual processing speed. Again, the specificity of the TVA method helped go beyond clinically based notions.

One TVA study has been conducted with a comparable design and size to the investigation by Habekost and Rostrup (2005a, 2005b). Peers et al. (in press) tested 25 patients using whole and partial report experiments and compared the results to MR scans of the lesions. Unlike Habekost and Rostrup, Peers et al. confined their study to focal cortical lesions in either the parietal or frontal lobe, without extensive subcortical involvement. Both left and right side damage was studied. A main result of Peers et al.'s investigations was that visual capacity (both *C* and *K* estimates) were reduced in patients with parietal lesions, but not after frontal lesions. More specifically there was a significant tendency that low visual capacity was associated with damage in relatively inferior parts of the parietal lobe, in the region of the temporo-parietal junction. On the other hand, deficits in top-down selectivity and asymmetries in attentional weighting correlated with simple lesion volume rather than with lesion location. No significant side differences in sensory effectiveness were reported, although the data indicated some asymmetry after right parietal lesions. Test performance generally did not depend on the side of the lesion, which is perhaps surprising given the traditional association of visual attention deficits (i.e., neglect) and right hemisphere damage. However patients were tested in the chronic stage of recovery, and neglect was generally weak or absent.

The results suggest that if performance is not confounded by neglect (which often implies deficient arousal) the TVA parameters depend on symmetrically distributed anatomical systems. However more studies are needed to confirm this hypothesis.

5.5) General evaluation of the method

As Cronbach (1959) noted, the quality of any test is relative to the purpose of the measurement. TVA based assessment is potentially useful both as a research tool and as a practical examination procedure in the clinic. Here, the focus is on the value of the method for research purposes (its clinical usability is currently being investigated by a group of neuropsychologists in Munich). The two issues are of course related, but an important difference is that practical assessment must be relevant to the patient's life in general, whereas for research purposes precise measurement of cognitive functions is an end in itself.

On four major parameters of test quality: validity, reliability, sensitivity, and specificity, TVA based assessment compares favourably to the clinical tests of visual attention used in much neuropsychological research. The strong grounding in basic cognitive theory is a core asset of the method. This ensures a firm connection to normal cognitive function, something that is less clear for most clinical tests. The fact that the parameters measured in TVA based assessment can also account for performance in a wide range of other experimental tasks strongly supports the method's general validity. Other aspects of validity were discussed in section 5.1.: The choice of stimulus material, the fact that only perception during single fixations is measured, the relation to other clinical tests, and the discriminant validity of the TVA parameters. Like all other test methods, TVA based assessment investigates cognitive function through a

particular set of procedures, which inherently limits the scope of the conclusions. In spite of these limitations, I have argued that basic, separate aspects of visual attention do seem to be measured. Although complex attentional phenomena (including motor exploration) are not described, the basic TVA measures should provide a good starting point for expanding the coverage of the assessment in the future.

As estimated by bootstrap statistics, the reliability of the test scores produced by the TVA method is generally high (with the notable exception of the α parameter). The inclusion of bootstrap analysis is in itself a major asset for the method, since information on the measurement error of neuropsychological tests has so far been available only through general norm sets of test-retest correlations. The bootstrap method may also be useful for investigations of sustained attention, an aspect of TVA based assessment that is largely unexplored at present. The method does however not address test-retest reliability, and since no norm sets for repeated test administrations have been produced, TVA based assessment is currently underdeveloped on this point.

High sensitivity is obtained by using computer generated displays with individually calibrated physical properties (e.g., exposure durations) to avoid floor and ceiling effects. In particular, the use of near-threshold stimulation seems to be an effective way of revealing subtle attentional abnormalities (Habekost & Bundesen, 2003). In addition, the high reliability of the method enables minor deviations from normal performance to be detected with statistical significance (Habekost & Bundesen, 2003; Habekost & Rostrup, 2005a).

A final quality of the method is its specificity. The functional analysis into five distinct parameters helps measurement go far beyond simple notions of “attentional deficit”. The fact that whole and partial report tasks include no significant motor

component is also important. This way performance should reflect specifically visual processes, something that is much harder to investigate from reaction time data. Preliminary data (Finke et al., submitted) suggest that inter-correlations between TVA parameters are generally low, indicating good discriminant validity. However TVA based assessment may have a problem separating *C* and *K* parameters. The moderate correlation between these two parameters could be caused by a general level of visual capacity that affects both *C* and *K* but varies individually. Alternatively, the correlation may be due to the analytical difficulty of separating the effects of the two parameters, particularly in subjects with low *C* values.

Ultimately the usefulness of the method for research purposes must be judged from the quality of the studies produced. Four studies have been conducted prior to or in parallel with the present project, all of them published in major journals. In the next chapter I present three new studies, aiming to further increase the credibility of the TVA method for neuropsychological research.

6. TVA BASED STUDIES OF RIGHT SIDE BRAIN DAMAGE

The main research contribution of the present dissertation is represented in three empirical articles. The articles describe how TVA based assessment was applied in a single case investigation and a group study of about 25 patients. Patients were examined for both lateralized and non-lateralized deficits, and their lesions were described using high-resolution MR scans. Together the studies provide an overview of the cognitive structure and lesion anatomy of visual attention deficits after right side stroke, from the new perspective of TVA measurement. In this chapter the findings are summarized and their contribution to general theory is outlined.

6.1) Summary of empirical studies

Using whole, partial, and colour report experiments *Habekost and Bundesen (2003)* tested a patient with hemorrhage in the right basal ganglia and overlying frontal cortex. The results were compared to an age-matched control group of eight participants. The patient showed no neglect in clinical testing, but had a subjective experience of slight attentional disturbance. The whole report experiment revealed a marked bilateral reduction of VSTM capacity in the patient, whereas processing speed in both visual fields was in the lower normal range. In addition the patient had elevated visual thresholds, with a non-significant trend towards higher thresholds in the left side. The possible asymmetry near the perception threshold was explored in a partial report experiment using very brief, post-masked displays. Under these conditions the patient performed clearly worse with unilateral displays in the left side, which was attributed to a higher visual threshold in this side. Testing with bilateral stimulation further revealed

that the patient had markedly lower attentional weighting in the left side. However no impairment of top-down selectivity could be demonstrated in either visual field, in spite of clearly reduced sensory effectiveness for colour in the left side (measured in a colour report experiment). Presenting a novelty in neuropsychological testing, the reliability of each TVA estimate was estimated by bootstrap statistics. The bootstrap analysis showed that parameter estimation was generally robust, though less so for α values. Overall the study extended the pioneer work of Duncan et al. (1999) and showed the strength of TVA based assessment in a single case, with a lesion in the anterior part of the brain, and only minor clinical symptoms. The fact that a range of attentional abnormalities could be demonstrated in a patient with no obvious clinical deficits suggested that subtle disturbances of visual attention are more common than usually assumed.

Habekost and Rostrup (2005a) followed up on the findings of Habekost and Bundesen (2003) in a large group study. Twenty-six patients with stroke in the right side of the brain were tested in whole, partial, and colour report experiments, and their performance was compared to twelve control participants. As expected, the results showed that persisting visual asymmetries are widespread after right side brain damage. The deficits were often minor, but the reliability of the individual findings was confirmed by bootstrap analysis, now refined to produce 95% confidence intervals for each estimate. Testing with unilateral displays revealed that visual thresholds were normal for all but a few patients, whereas visual processing speed was consistently reduced in the left side. Voxel-based lesion analysis linked the asymmetry in visual processing speed to damage in the putamen, which occurred with high frequency in the patient group. Additional cortical damage did not exacerbate the asymmetry, and patients with focal thalamic or cortical lesions were generally not affected. A different

pattern was revealed in case of bilateral stimulation. Attentional weighting of the left visual field was generally reduced in patients with large lesions, but rarely after focal lesions. However, a single thalamic patient showed a clear extinction-like pattern. By subtracting the lesions of three other thalamic patients who had normal attentional weighting, the patient's deficit was linked to damage in the lateral pulvinar. The finding agrees closely with the location of a general saliency map proposed in the neural TVA theory. In the patient group as a whole top-down selectivity was poorer in the left side, in spite of symmetrical colour perception (i.e., target-distracter discriminability) as measured by colour report. There was however considerable variability among patients, and a correlation between the asymmetry of α values and lesion volume fell short of significance. In general, the study showed that side differences in visual perception are common after right side brain damage, even in patients who are in the stable phase of recovery and show minor or no neglect. Two main types of visual asymmetry were described: One related to sensory effectiveness (unilateral displays), the other to attentional weighting (bilateral displays). The two deficits were mapped to distinct patterns of brain injury.

Habekost and Rostrup (2005b) analyzed test results from the same data set as Habekost and Rostrup (2005a), but focused on deficits in the general capacity of visual attention. Both VSTM storage capacity and ipsilesional processing speed were preserved in most patients, even after large cortical lesions. Lesions mainly affected anterior regions in the right side of the brain, indicating that these areas are not critical for VSTM capacity or ipsilesional processing speed. The finding is consistent with a parallel TVA study by Peers et al. (in press), who found that frontal lesions were not related to general reductions in attentional capacity. Another result in line with Peers et

al. was that damage in the temporo-parietal junction was related to reduction of ipsilesional processing speed. In addition, Habekost and Rostrup found that VSTM capacity was consistently reduced after severe leukoaraiosis or very large strokes extending deep into the posterior white matter. Leukoaraiosis was also related to bilateral deficits in visual processing speed, though with larger individual variations. Overall, the study pointed to the critical importance of cerebral connectivity for the general capacity of visual attention.

6.2) Conclusion

Equipped with a new assessment method, the Ph.d.-project set out to study visual attention deficits after right side lesions. Although based on previous cognitive and neuropsychological research, the novelty of the assessment procedure essentially made the project explorative. Not much was known in advance on the relation between different types of right side brain damage and the TVA parameters. The exploration led to several discoveries of general interest, both in terms of methodology and empirical findings.

The methodological contributions of the Ph.d.-project consisted in further developments of the TVA based assessment method presented by Duncan et al. (1999). Whereas Duncan et al. studied patients with marked clinical deficits (i.e., neglect), Habekost and Bundesen (2003) showed that TVA based assessment can detect attentional deficits in patients with only minor clinical problems, and thus highlighted the *sensitivity* of the method. Habekost and Rostrup (2005a) firmly established this point in a large group of patients. Another main development was the introduction of bootstrap analysis. The idea of using bootstrap statistics for estimating the measurement

error of TVA estimates was proposed by C. Bundesen, and S. Kyllingbæk has made important contributions including a software package (www.psy.ku.dk/cvc) and theoretical explorations of the method using simulated data. However the specific application of bootstrapping as a neuropsychological research tool was developed within the present Ph.d.-project. Bootstrap analysis provides information that was previously not available in neuropsychological assessment: the measurement error related to individual test results. This development fits nicely with the recent emphasis on test sensitivity: Small abnormalities at single case level can now be given a refined quantitative evaluation (e.g., intra-individual significance tests; Habekost & Rostrup, 2005a) to determine their reliability.

Besides these methodological developments, several of the empirical findings should be relevant to general theoretical issues. Habekost and Rostrup (2005a) showed that different forms of visual asymmetry very often persist into the chronic stage after right side stroke. Strict epidemiological selection was not used, but the findings were highly consistent across more than twenty patients with stroke in the middle cerebral artery. The asymmetries occurred even though most patients showed no clear signs of neglect or extinction in standard tests. The results suggest that neglect and extinction (as clinically defined) represent only the tip of the iceberg for visual asymmetries, and that more subtle disturbances are highly common after right side brain damage. Given testing that is sensitive enough, it seems that (slightly) impaired visual processing in the left side can be demonstrated for a very large percentage of such patients. Until now these “subclinical” deficits have largely passed under the radar of neuropsychological assessment, but their existence has now been established. Future studies should clarify the clinical relevance of these subtle abnormalities.

Although the experimental tasks included no significant motor component, performance asymmetries also occurred after selective damage in areas that are traditionally related to movement, such as the frontal lobe and basal ganglia. In fact, Habekost and Rostrup (2005a) found that the most critical area for asymmetries in sensory effectiveness was located in the posterior putamen. Also the patient tested by Habekost and Bundesen (2003) had damage confined to anterior brain structures, which are usually not associated with basic visual functions. These findings are in line with theories that criticize the traditional strong division of perceptual and motor function (Allport, 1987; Hommel, Müsseler, Aschersleben & Prinz, 2001; Neumann, 1987). Instead the results support the notion that visual and motor functions are deeply interwoven, reflecting strong reciprocal connections in the anatomical networks for visual attention that span posterior and anterior regions of the brain.

Attentional weighting (or bias) is a central concept in contemporary theories of attention (e.g., Desimone & Duncan, 1995), and the extinction phenomenon has often served as a model phenomenon. The results of Habekost and Rostrup (2005a) pointed to an anatomical basis for the extinction mechanism that is both localized and distributed. Selective disturbance of attentional weights in the left hemifield was found after pulvinar damage, closely following the predictions of the neural TVA theory (Bundesen et al., in press). On the other hand, extinction-like effects were also associated with large lesions, which supports a more anatomically distributed account of spatial bias (Duncan, 1999). The results are however compatible. In the neural TVA theory the (localized) saliency map summarizes activity from many (distributed) cortical areas, which should make its function vulnerable to both types of damage. The results of Habekost and Rostrup (2005a) also bear on the notion that extinction is related to

reductions in general attentional capacity (Marzi et al., 2001). Whereas this may be necessary for extinction to occur in the clinical confrontation test, Habekost and Rostrup showed that clear spatial bias also occurs in patients with normal (VSTM) capacity, provided that the stimulus display is complex enough to potentially fill up VSTM.

Habekost and Rostrup (2005b) drew attention to the importance of white matter connectivity for general attentional capacity. Functional imaging studies have emphasized the involvement of the (posterior parietal) cortex, but it seems that the underlying fibres are just as relevant. This hypothesis is in agreement with theories that conceive visual consciousness and short-term memory as products of large-scale interactions between multiple brain areas (Crick & Koch, 1995; Duncan, 1996) linked together by fast, efficient connections. The study of Habekost and Rostrup may serve the same purpose as Habekost and Bundesen (2003), and lead to a more powerful follow-up study that examines the connectivity issue in a larger, more targeted patient group. Investigations of patients with varying degrees of leukoaraiosis seem well suited for this purpose.

Perhaps the main contribution of the project was that, compared to a few years ago, we now have the outlines of a general mapping of critical brain areas for the various TVA parameters. Equal credit for this achievement should be given to the patient study by Peers et al. (in press) that was conducted in parallel. Together these two projects have examined more than 50 patients with unilateral brain damage, which has produced converging evidence on several points: Large unilateral lesions are related to ipsilesional biases in attentional weighting, but unilateral lesions in anterior regions of the brain are not critical for VSTM capacity or visual processing speed outside the contralesional field. In addition, both studies found some evidence that the TPJ region is

important for general visual processing speed, though more data is needed on this issue. Another main finding is that the putamen area is important for contralesional processing speed, whereas focal lesions in the thalamus or posterior cortex seem to have little effect on this parameter (Habekost & Rostrup, 2005a). In the quest to map the anatomical basis of the TVA parameters, much still remains to be done. The most obvious questions derive from suggestive findings in the two research projects. The importance of the pulvinar nucleus for attentional weighting (Habekost & Rostrup, 2005a) should be confirmed in a study of more thalamic patients. The role of the posterior white matter for general attention capacity (Habekost & Rostrup, 2005b) should also be followed up, perhaps by exploring the relation to leukoaraiosis. Finally, only about a fourth of the patients in the two projects had left hemisphere damage. Contrary to influential theories of right hemisphere dominance for visual attention, Peers et al. found that damage in the left side of the brain led to equal impairment. The function of the left hemisphere should be further investigated in a TVA context.

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PERSISTING ASYMMETRIES OF VISION AFTER RIGHT SIDE LESIONS

Thomas Habekost

Center for Visual Cognition, Department of Psychology, University of Copenhagen

Egill Rostrup

Danish Research Centre for Magnetic Resonance, Hvidovre Hospital, Copenhagen

Abstract

Visual neglect and extinction are well-known effects of lesions in the right hemisphere. This study shows that even with minor or no clinical signs of these deficits, and in the stable phase of recovery, asymmetric visual perception is common after right side lesions. Whole, partial, and colour report experiments were used to estimate psychophysical parameters related to visual capacity and attentional weighting in 26 patients with stroke in the right side of the brain. The results were analyzed using Bundesen's Theory of Visual Attention (TVA; Bundesen, 1990) including bootstrap estimation of the measurement error related to each test result (Habekost & Bundesen, 2003). Lesions were examined by MR scanning and analyzed statistically. Two main types of deficit were found. The first type was related to perception of unilateral displays, where most patients showed left side reductions of visual processing speed. This visual asymmetry was linked to a highly frequent affection of the putamen and surrounding white matter. The second deficit type occurred with bilateral displays, which increased the visual asymmetry (extinction effect) for most patients with large cortico-subcortical lesions, but rarely for patients with focal lesions. However in a single case with pulvinar damage, visual asymmetry occurred selectively with bilateral stimulation. Overall, the study provided an overview of the cognitive structure and lesion anatomy of subtle visual asymmetries after right side stroke.

1. Introduction

Visual extinction is defined as a condition in which a contralesional stimulus is perceived normally when shown in isolation, but missed ("extinguished") when accompanied by an ipsilesional stimulus (Bender, 1952). Visual neglect is defined by a similar bias towards the ipsilesional field, but is a more complex syndrome where multiple aspects of space representation and exploration are typically also disturbed (Karnath, Milner, & Vallar, 2002). Extinction is often considered a mild form of neglect (Heilman, Watson, & Valenstein, 2003) but double dissociations have been reported between the two conditions (Cocchini, Cubelli, Della Sala, & Beschin, 1999), and the lesion anatomy may also differ (Karnath, Himmelbach, & Küker, 2003; Vallar, Rusconi, Bignamini, Germiniani, & Perani, 1994). The two syndromes should therefore be regarded as partly independent. Neglect is a common finding in the acute stage, with up to half or more of patients with right hemisphere stroke showing some sign of the condition (depending on the assessment procedure: Azouvi et al., 2002), but it has been argued that neglect rarely persists into the stable phase of recovery (Maguire & Ogden, 2002; Stone, Patel, Greenwood, & Halligan, 1992) especially in the absence of field cuts (Samuelsson, Jensen, Ekholm, Naver, & Blomstrand, 1997). However this conclusion is based on performance with standard clinical tests such as line bisection and visual cancellation, and subtle attentional biases may still be revealed in the pattern of eye movements (Olk, Harvey, & Gilchrist, 2002), judgment of brightness gradients (Mattingley et al., 2004), or daily life behaviour (Azouvi et al., 2002). Thus minor abnormalities can persist even though most patients eventually recover from or compensate for their initial marked symptoms. Visual extinction is also relatively common in the acute stage (Vallar et al.,

1994: 16% of a consecutive series of right side lesions), and clinical experience suggests that the condition tends to be chronic (Heilman et al., 2003). However systematic investigations of the long-term prevalence of extinction have not been conducted. As with neglect, the prevalence may be underestimated due to low sensitivity of the standard clinical test (detection of unilateral versus bilateral finger movements). Therefore it is possible that many patients who apparently have recovered from neglect or extinction, or perhaps never been diagnosed with these conditions, in fact continue to have visual asymmetries in a milder form.

To control better for ceiling effects in performance, a number of recent studies have tested neglect and extinction patients using computer based experiments that enable individualized, near-threshold stimulation. A main result of these investigations is that contralesional stimuli are often perceived abnormally even when presented alone (i.e., without competing stimuli in the ipsilesional field) suggesting that sensory effectiveness is compromised unilaterally. Especially in case of extinction this runs counter to traditional notions. Both extinction and neglect can occur without damage in the primary visual pathways, and by definition cannot be attributed to sensory or motor defects (Heilman et al., 2003). It is often assumed that unilateral displays are processed normally and that bilateral stimulation (or in case of neglect: tasks involving space exploration) is necessary to bring out the right side advantage (Karnath, 1988). Both behavioural and electrophysiological evidence now makes this assumption untenable. In a group of patients with right side lesions, Smania et al. (1998) found that both reaction time (RT) and detection rates were impaired for single brief flashes of light in the contralesional compared to the ipsilesional hemifield. The interfield difference was greatly pronounced for patients with neglect; extinction patients showed a smaller effect. Marzi et al. (1996)

also found slowing of RT to contralesional flashes, and Angelelli, de Luca, and Spinelli (1998) reported decreased contrast sensitivity contralesionally in neglect patients, but normal performance in other patients with right side lesions. In addition to these behavioural demonstrations, evoked response potential studies have revealed abnormalities in the neural response to single contralesional stimuli in patients with neglect (Angelelli, de Luca, & Spinelli, 1996; Spinelli, Burr, & Morrone, 1994; Spinelli, Angelelli, de Luca, & Burr 1996) and extinction (Marzi, Girelli, Natale, & Miniussi, 2001). In summary there is now solid evidence that processing of single contralesional stimuli is abnormal in neglect and, probably to a lesser extent, extinction patients. However it has not been demonstrated that the asymmetry extends to right damaged patients with minor or no clinical signs of attentional deficit.

We aimed to test the hypothesis that impaired sensory effectiveness in the contralesional field is common after right side brain damage, even for patients in the stable phase of recovery with no clear symptoms of neglect or extinction. We also wanted to explore the prevalence of rightward attentional biases (extinction-like effects) in this group. To obtain a comprehensive picture of the patients, we included measures of attentional control and general capacity, as well as detailed lesion analysis. As in the above mentioned studies we used stimulation near perception threshold for sensitive testing. However the previous investigations were extended in a number of ways. First, we selected patients by a broad anatomical criterion (damage in the right side of the brain) and not by clinical symptoms of attention deficit. As patients were also in the stable phase of recovery ($\geq$ 6 months post-injury), most showed only minor or no clinical signs of neglect or extinction. This in effect focused the study on sub-clinical deficits. Second, to minimize motor involvement and biases in space exploration, we studied perception

within the time frame of a single fixation, arguably the basic element of vision. Unlike the RT experiments described above our tasks involved no significant motor component, but only required unspeeded report of perceived items. This should make findings specific to the visual system and not confounded by asymmetrical motor biases or general slowing of response. Third, we based the analysis of the experimental data on the Theory of Visual Attention (TVA) developed by Bundesen (1990). This enabled us to analyze performance into a number of parameters related to sensory effectiveness, perception thresholds, attentional weighting, and visual short-term memory capacity, and thus to identify specific components in the visual asymmetries. By measuring this range of visual parameters in each patient we were able to address hypotheses on the relation between extinction and general attentional capacity (Husain, Shapiro, Martin, & Kennard, 1997; Karnath, 1988; Mattingley, 2002) and the relation between sensory effectiveness and extinction (Marzi et al., 2001). Another strength of TVA analysis is that it can be coupled with statistical bootstrap methods to estimate the measurement error related to each test result (Habekost & Bundesen, 2003), which is very useful for investigating minor abnormalities. As a final feature the study included high-resolution MR scans of each patient, which were used for statistical lesion analysis.

1.1. Theory of visual attention (TVA)

The TVA theory forms a basic analytic frame for our study. The theory was presented by Bundesen (1990) and accounts for findings from a wide range of experimental paradigms such as single-stimulus recognition, whole report, partial report, detection, and visual search (for a recent review of TVA and the attention literature, see Bundesen & Habekost, 2005). The model has also been integrated with theories of

memory, categorization, and executive function (Logan, 2002; Logan & Gordon, 2001). Whereas the original TVA model was framed at a cognitive description level, its principles have recently been shown to have a strong analogy at the single cell level (Bundesen, Habekost, & Kyllingsbæk, in press). The principles of TVA were introduced in a neuropsychological context by Duncan et al. (1999), who studied a group of neglect patients. Since then the method has been shown to possess the sensitivity and specificity necessary for single case studies (Duncan et al., 2003) even with patients who have only minor attentional problems (Gerlach, Marstrand, Habekost, & Gade, in press; Habekost & Bundesen, 2003; Peers et al., in press).

TVA is a computational model that describes visual recognition and selection in terms of five parameters, whose relation is given by a set of equations (see Appendix for mathematical details). These parameters are: (a) the *perceptual threshold*, t_0: the shortest exposure duration at which visual identification is possible, (b) the *visual processing speed*, C: the total number of visual elements processed per second, (c) the *storage capacity of visual short-term memory* (VSTM), K: the maximum number of objects that can be reported from a brief visual display, (d) the *visual selectivity*, α: the ability to focus on targets rather than distractor objects, and (e) the *spatial bias*, w_{index}: the relative attentional weighting of stimuli in different parts of the visual field (here: left vs. right). t_0, C, and K can be estimated in *whole report* experiments (see section 3.1), and α and w_{index} can be inferred from *partial report* data (see section 3.2). When unilateral displays are used, estimates of t_0, C, K, and α can be obtained separately in each visual field, whereas w_{index} by definition relates to bilateral displays. In experiments that use only one exposure duration (as our partial report study) the processing rate C cannot be inferred

from the data. Instead the *accumulated sensory effect*, *A*, of the display can be estimated. *A* is an indirect measure of sensory effectiveness.

2. Methods

2.1. Subjects and clinical investigation

Medical records of all patients admitted to a brain injury rehabilitation centre (during a period of three years) and two university hospital stroke units (during a period of approximately two years) in Copenhagen were screened for radiological evidence (CT or MR) of stroke in the right side of the brain. To be selected for participation, a patient should also be at least six months post-injury and satisfy the following inclusion criteria: (a) normal visual acuity (Snellen score $\leq$ 9/6) and no field cuts, (b) no dementia (MMSE score $\geq$ 24), (c) no aphasia, (d) no history of major psychiatric or other neurologic disease, (e) no substance abuse, (f) age $\leq$ 70 years,[1] (g) no oculomotor abnormalities, (h) auditory span of at least four elements, and (i) no additional damage in the left side of the brain.[2] All patients who satisfied these criteria were invited to participate in the study; twenty-four patients agreed. In a second round of selection the patient panel at the Cognition and

[1] In the initial phase of the project two patients aged above 70 years were examined, because at this point it was unclear whether enough patients could be recruited. Independent of focal lesions, general processing capacity may be affected by non-specific factors related to aging. However the relative pattern of performance in the left vs. right visual field should not be affected by such general reductions of capacity. Since the present study deals mainly with relative asymmetries and not absolute levels of performance, we chose to keep the data of these two patients in the analysis.

[2] After the psychophysical examination had been conducted, the MR scan of two patients revealed strokes in the left side of the brain. The data from these patients were excluded from the analysis. In another patient there were lacunar infarctions in the left basal ganglia and right pons. This patient (with a selective impairment of attentional weighting after right pulvinar damage) was however deemed so interesting that his data was included in the project (patient "T3"). If anything, the small infarct in the left side should have countered his extinction tendency. In five patients varying degrees of leukoaraiosis (diffuse white matter abnormalities) was detected. Similar to other factors related to aging, this may have reduced the general capacity of these patients. However the white matter abnormalities were bilateral and symmetric, so the reduction should affect either visual field equally (cf. footnote 1). The data of these patients were included in the analysis.

Brain Sciences Unit in Cambridge was searched for individuals with focal basal ganglia lesions. One patient was included in the project, but only tested in the partial and colour report experiments. In a final round of selection one year of medical records from a hospital stroke unit in Copenhagen were screened for patients with focal lesions in the thalamus, which lead to the participation of one additional patient. All patients gave informed written consent according to the Helsinki Declaration, and approval was given by ethical committees in Copenhagen City and Copenhagen County (project no.: KF 01-116/02). The mean age of the patients was 56.6 years (*SD* = 9.9 years), and the group consisted of 12 men and 14 women. Time post-injury ranged from 6 to 91 months (mean: 22 months). All patients except three were right handed according to the Edinburgh Handedness Inventory. Twelve neurologically healthy participants formed an age-matched control group (5 men and 7 women; mean age: 56.6 years, *SD* = 5.4 years).[3] The controls were recruited by local advertisements and paid for their participation, and also gave informed written consent. In addition to the psychophysical testing, participants were given a screening battery of neuropsychological tests: Snellen chart, MMSE (patients only), Weintraub and Mesulam's (1985) cancellation test (letters and figures, unstructured versions), Wilson, Cockburn, and Halligan's (1987) line bisection test, Rey Figure Copying, auditory span, Edinburgh Handedness Inventory, and an extinction test (detection of finger movements unilaterally vs. bilaterally). Visual fields were assessed by confrontation (patients only). See Table 1 for clinical and demographic characteristics of the patients.

[3] The data from two control participants were excluded because of a consistent failure to comply with the instructions, and use of strong analgesic medication during testing, respectively.

Table 1: Demographic and clinical characteristics

Subj	Age/Sex	Aetiology	Volume	Extinction	Bisection	Rey	Cancel
Large lesion group							
L1	43/F	Haemo	47	2 / 10	-1	1	6:4, 3:0*
L2	70/M	Infarct	31.5	1 / 10	-6	0	0:0, 0:0
L3	58/F	Infarct	63.9	1 / 10	+9	-	1:0, 0:2
L4	45/M	Haemo	95.9	1 / 10	-8	0	0:0, 0:0
L5	53/M	Haemo	167.7	2 / 10	-15*	0	0:1, 1:0
L6	68/F	Infarct	137.5	9 / 10*	+7*	0	6:2*, 1:0
L7	44/F	Infarct	189.9	0 / 10	-1	0	3:1, 4:0*
L8	57/M	Infarct	142.7	-	-4	0	1:0, 1:0
L9	39/F	Infarct	-	0 / 10	+1	0	0:1, 0:0
L10	46/F	Infarct	153.3	3 / 10	+3	1	2:1, 1:0
L11	58/M	Infarct	35.1	8 / 10*	-2	1	3:1, 3:1
L12	54/F	Infarct	58.8	2 / 10	-1	-	1:0, 0:2
L13	47/F	Infarct	232.9	2 / 10	+2	0	3:0*, 0:0
L14	63/M	Infarct	214	1 / 10	-13*	0	1:1, 2:2
Basal ganglia group							
B1	50/M	Infarct	0.6	0 / 10	+4	1	0:0, 1:0
B2	50/M	Infarct	0.6	0 / 10	+1	0	1:1, 3:6
B3	65/F	Haemo	2.5	0 / 10	-2	0	0:0, 0:0
B4	66/M	Haemo	13.6	3 / 10	+2	0	2:2, 3:0*
B5	61/M	Haemo	-	0 /10	-6	0	0:0, 0:0
Thalamus group							
T1	56/M	Infarct	0.5	0 / 10	+1	0	0:0, 0:0
T2	46/F	Infarct	0.1	0 / 10	-11*	0	0:0, 0:0
T3	54/M	Haemo	1.0	0 /10	+2	0	0:0, 0:0
T4	68/F	Haemo	2.0	0 /10	+1	-	0:0, 0:1
Focal cortical group							
FC1	66/F	Infarct	-	1 / 10	+5	0	4:0*, 0:0
FC2	73/F	Infarct	19.9	1 / 10	-1	0	0:0, 2:1
FC3	71/F	Haemo	8.6	-	-	-	-

**: abnormal performance; Subj: subject; Aetiology: haemorrhage or infarct; Volume: lesion volume (cm^3; missing for CT scans); Extinction: frequency of left side omissions with bilateral stimulation; Bisection: average rightward deviation (mm) from centre on Wilson et al.'s (1987) line bisection test; Rey: number of left side omissions on Rey Figure Copying; Cancel: number of left vs. right side omissions on Weintraub & Mesulam's (1985) cancellation test (figures and letters versions, respectively).*

Only two patients qualified for visual extinction according to the criteria used by Vallar et al. (1994): >30% left side misses with bilateral stimulation, but >80% correct reports of single left side stimuli. However twelve other patients had between one and three left side misses out of ten bilateral stimulations (whereas unilateral stimulation was nearly always detected), which can be considered borderline or subclinical signs of extinction. Likewise, only a minority of patients showed significant neglect on standard tests: line bisection (at least two out of three deviations of more than 12.75 mm from the midpoint), visual cancellation (at least three targets missed on the contralesional side relative to the ipsilesional side) or figure copying (more than one left-side omission). However many patients had smaller abnormalities in their test performance. Thus subtle signs of neglect or extinction were common throughout the group, but apart from a few cases the deficits were not clinically significant.

2.2. Experimental procedure

The experiments were set up using E-prime software (version 1.1) and run on an IBM-compatible computer. Participants were seated with their eyes approximately 100 cm from the screen in a semi-darkened room. Visual stimuli were shown on a computer monitor capable of 200 screen refreshes / second. Depending on the experimental condition, three or five letters were selected randomly and without replacement from the set {ABEFHJKLMNPRSTWXYZ} and flashed for 5 - 200 ms on the screen, followed by either a blank screen or a 500 ms bright pattern mask. Each letter was shown in one of ten possible positions at the circumference of an imaginary circle centered at fixation. The radius of the circle was approximately 5 visual degrees (viewing distance was not precisely controlled). The letters were either green or purple (with equal luminance: 36

cd/m^2); the colour was selected randomly for each letter. Report of the letters was unspeeded. The error rate was recorded continuously and given as feedback after each testing block. A score of 80 - 90% was encouraged. Percentage correct was on average 86.8 % (*SD* = 4.7 %) and 87.1 % (*SD* = 5.0 %) in the control and patient groups, respectively. Testing was divided into 300 trials of whole report, 300 trials of partial report, and 60 trials of colour report. The trials were organized in blocks of 50 or 60 trials, and all testing was completed within two or three sessions of maximally one hour's length including breaks. In addition, participants were given 20 - 30 unscored warm-up trials at the beginning of each session. The display side, and the exposure duration in the whole report experiment, was randomized.

To ensure central fixation before stimulus exposure in each trial, participants were instructed to look at a centrally placed cross and, after having signalled ready, to name a random digit that appeared for 300 ms at this position. Immediately afterwards the stimulus display was initiated by the experimenter. The instruction to fixate centrally was emphasized throughout testing. As an additional control the eye movements of all participants were recorded by a video camera, and the signal was mixed with a simultaneous camera recording of the computer display. The experimenter monitored the subject's eye movements continuously on a TV screen during testing, and the mixed image was recorded on VHS tape. The VHS tapes were subsequently inspected for unwanted eye movements (i.e., away from the central cross before stimulus exposure) using 32 random samples for each participant. If an unwanted eye movement was detected in any of these 32 trials, the whole VHS tape was inspected and all invalid trials removed from the data set. This was done for two patients, who had 96 trials and 40 trials,

respectively, removed from their data.[4] Eye movements of a single patient who was tested outside the laboratory were monitored directly by an experimenter. Three trials were removed from this data set.

In the *whole report* experiment, five letters were shown either to the left or right of fixation (see Figure 1a). Participants were instructed to report as many letters as possible, but refrain from guessing. The exposure duration was varied systematically, with six individually set exposure durations (based on performance in the practice trials). Four masked exposures were used, spanning an interval from the participant's approximate threshold (20 - 40 ms) to 200 ms. To prolong the effective exposure duration, two unmasked displays (usually 100 and 200 ms) were also used. There were 25 repetitions for each of these 2 * (4 + 2) = 12 conditions, randomly intermixed within each testing block.

In the *partial report* experiment, participants were instructed to report as many letters as possible with a pre-specified target colour (green or purple), but refrain from guessing. The target colour alternated between each testing block. To ease identification of colours, stimuli were shown unmasked. Testing was divided into five conditions of 60 trials each, which were randomly intermixed within each testing block. In the first two conditions, stimulation was confined to either the left or right visual field, where three targets were shown (see Figure 1b). In two other conditions, the three targets were accompanied by two distractors of the non-target colour (see Figure 1c). The position of each letter was chosen randomly from the five possible in each side, so targets and distractors were mixed in an unpredictable fashion. In the fifth ("extinction") condition, five targets were shown at random positions out of the 10 possible. This typically resulted

[4] The video recording of one of these patients' partial and colour report testing was deleted by mistake. However this patient's perception was generally symmetrical and the removal of trials from her whole report data only changed test results very slightly.

in bilateral stimulation (see Figure 1d). One exposure duration was used throughout the experiment (5 – 200 ms), calibrated individually to avoid ceiling or floor effects on performance.

In the *colour report* experiment, five letters (each randomly coloured green or purple) were shown to either the left or right (cf. Figure 1a), with the same individually set exposure duration as in partial report. The instruction was forced-choice naming of the colour (either green or purple) of each of the five shown letters, starting from the top of the semi-circle. One block of 60 trials was given[5].

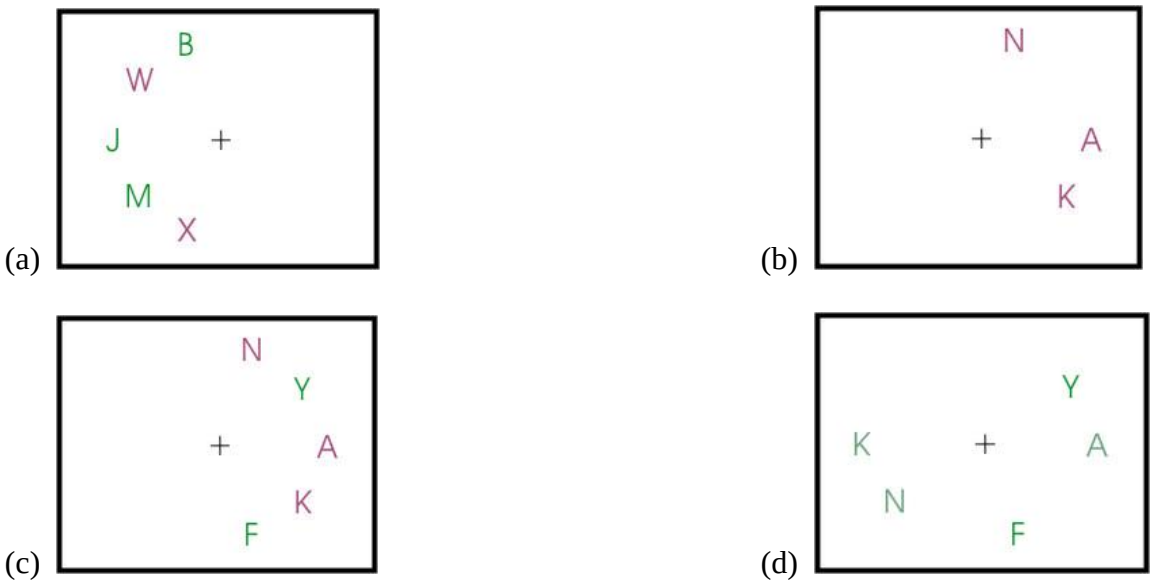

Figure 1. *Experimental displays. (a) Whole report: five letters were presented either to the left or right of fixation. (b) Partial report, unilateral target-only condition: Three letters with the target colour (here: purple) were presented in one side. (c) Partial report, distracter condition: Three targets were accompanied by two distracter letters of a different colour (here: green) in the same side. (d) Partial report, bilateral target-only condition: Five target letters (here: green) were presented in random positions across the left and right visual field.*

[5] Due to an error of administration, one patient only performed 30 colour report trials.

2.3. Data analysis

The best-fitting TVA parameter values to the observed data of each participant were estimated by a maximum likelihood fitting algorithm. The model fitting procedure used to analyze the results was basically the same as that employed in previous TVA studies, and we refer to Duncan et al. (1999) for mathematical details. Customized software for TVA analysis developed by S. Kyllingsbæk (www.psy.ku.dk/cvc/tva) was used, which also allowed for bootstrap analysis of the fits (see Habekost & Bundesen, 2003; also see Chernick, 1999; Efron, 1979; Efron & Tibshirani, 1993). The following parameters were estimated. In whole report: K, C_{left}, C_{right}, $t_{0\text{left}}$, $t_{0\text{right}}$, and μ, and in partial report: A_{left}, A_{right}, α_{left}, α_{right}, w_{left}, w_{right}. Since only one exposure duration was used in partial report, the VSTM limit could not be estimated directly in this experiment. Instead we used a plug-in estimate of VSTM capacity, K', given by the frequency-weighted average of the highest and next-highest score obtained by the participant (Peers et al., in press). To make the model fitting more robust t_0 values were constrained to be 15 ms at minimum. K values were constrained not to be higher than the best score obtained by the participant. All observed data was included in the analysis (no exclusion of outlier trials). The reliability of each parameter estimate was evaluated by 1000 bootstrap repetitions, a sample size that allows for construction of confidence intervals (Efron, 1987). Each bootstrap sample was constrained to include at least one trial with the subject's maximum score.

2.4. Lesion analysis

The lesions of all patients except three were identified by MRI. 18 patients were examined in a 3T scanner (Siemens Trio), and 5 patients were examined in a 1.5 T scanner (Siemens Vision). For a high precision description of the structural anatomy, a 3D volumetric MPRAGE sequence (1 mm^3 resolution; 3T: TR/TE/TI: 6.0/3.93/800 ms, flip angle: 8 deg; 1.5T: TR/TE/TI: 13.5/7 /100 ms, flip angle: 15 deg) covering the whole brain was performed. To characterize the lesions in further detail, patients were also examined using supplementary FLAIR sequences (3T: TR/TE/TI: 9000/102/2500 ms, flip angle: 150 deg; 1.5T: 9000/110/2400 ms, flip angle: 180 deg). Using the combined information from these scans, the lesions were drawn on each individual's MPRAGE slices by an experienced neurologist who was blind to the psychophysical data. Besides tracing the haemorrhage or infarct, leukoaraiosis (visible on the FLAIR scans) was also noted if present. The MPRAGE scans with traced lesions were normalized to a 1 mm isotropic T1 template using SPM2 (www.fil.ion.ucl.ac.uk/spm/software/spm2). Before normalization the lesion area was masked out from the intact part of the brain to prevent distortions (Brett, Leff, Rorden, & Ashburner, 2001). The volume of the (normalized) lesion was computed using the MRIcro program (Rorden & Brett, 2001; www.mricro.com), and subtraction analysis was also carried out using this software (Karnath, Himmelbach, & Rorden, 2002). Voxelwise statistical testing was performed to locate areas significantly related to abnormal performance. For each brain voxel patients were divided into two groups, either with or without damage in the voxel. The psychophysical scores of these two groups were compared using a Wilcoxon test with significance threshold of $p = 0.01$ (not corrected for multiple comparisons). CT scans from the acute phase of three patients were collected from hospital records. The CT scans were

not analyzed quantitatively, but a verbal description was given by the examining neurologist. On the basis of their lesions, each patient was assigned to one of four subgroups: (a) large (volume > 25 cm^3) cortico-subcortical lesions in the territory of the middle cerebral artery (n = 14), (b) focal lesions in the basal ganglia and deep white matter (n = 5), (c) focal thalamic lesions (n = 4), and (d) focal cortical lesions (n = 3).

3. Results

In this section we present psychophysical results (TVA estimates) obtained from whole and partial report experiments, and relate this set of findings to lesion anatomy. Most TVA parameters were estimated separately in the two visual fields. To evaluate the symmetry of two particular values a lateralization index was computed using the formula $X_{index} = X_{left} / (X_{left} + X_{right})$, where X may stand for C, w, or some other TVA parameter. A lateralization index value of 0.50 indicates perfect symmetry between the two estimates in each side, whereas a value below or above 0.50 indicates a lower estimate in the left or right side, respectively.

The reliability of each estimate was quantified by bootstrap analysis. The bootstrap method supplies information that is rarely available in neuropsychological studies: A quantitative estimate of the measurement error related to each test result. This is especially useful when investigating small deficits on single case level (Habekost & Bundesen, 2003), where it is crucial to show that a given test result did not occur by chance. Given a set of observations (e.g., the 300 trials in whole report), bootstrap analysis computes the probability that an underlying parameter value is located in a certain interval. Consider for example the C_{index} value of a representative patient in the large

lesion group. TVA analysis estimated this parameter to be 0.39, indicating clearly faster processing in the right visual field. However could these whole report data have been produced by a person with a C_{index} value of 0.50, that is: equal processing speed in both visual fields? Bootstrap analysis allows us to reject this null hypothesis. Figure 2 shows how the bootstrap estimates of the patient's C_{index} were distributed. The estimates were close to normally distributed around the C_{index} value found in the original fit: 0.39, with a standard deviation of 0.023. This implies that with 95% confidence (i.e., plus/minus 1.96 standard deviations from the mean), the patient's C_{index} was located in the interval [0.34; 0.43]. This way the bootstrap method allows us to evaluate the precision of test results on single case level. Specifically, if the 95% confidence interval for a given lateralization index does not contain the value 0.50, the estimate is significantly different (at $p < 0.05$) from symmetric performance.

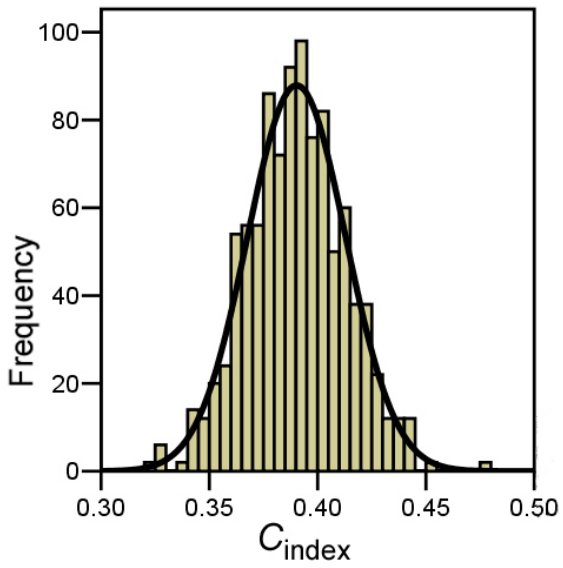

Figure 2. *Distribution of 1000 bootstrap estimates of C_{index} for a representative patient (L4). Solid curve indicates normal distribution. The 95% confidence interval was $0.34 < C_{index} < 0.43$.*

3.1. Experiment 1: Whole report

Whole report is a classical technique for estimating the total amount of available processing capacity (Cattell, 1885; Sperling, 1960). In TVA terms, total capacity is represented by parameters *C* (total processing speed) and *K* (maximum storage capacity of VSTM). In a typical whole report experiment the subject tries to report as many items as possible from a briefly exposed array of unrelated stimuli (e.g., letters). Performance (number of correctly reported items) is measured as a function of exposure duration, and follows a characteristic pattern (Bundesen & Harms, 1999; Duncan et al., 1999; Habekost & Bundesen, 2003; Shibuya & Bundesen, 1988; see also Figure 4). Below a minimal exposure duration, t_0, no items are reported. Above this exposure duration the curve rises sharply, but gradually flattens out over the course of a few hundred milliseconds. Given long enough exposure time performance approaches an asymptotic value, usually interpreted as the maximum storage capacity of VSTM: *K*. Data fits of this parameter are improved by using non-integer values. For example, a *K* value of 3.3 represents a probability mixture of VSTM capacity at 3 and 4 elements, occurring with 70% and 30% probability, respectively. The *C* parameter is a measure of the total processing speed during visual recognition, and corresponds to the slope of the whole report function at $t = t_0$. *C* is highly dependent on the sensory properties and general discriminability of the stimuli. When stimuli are presented unmasked, the effective exposure duration is prolonged by a constant, μ (Bundesen, 1990). This parameter is necessary for curve fitting, but will not be receive independent interest. Given a sufficient number of observations at different exposure durations, ranging from near-threshold to near-ceiling performance, these TVA parameters can be estimated from whole report data.

For a summary of the whole report fits, along with bootstrap estimations of the standard error related to each measurement, see Table 2. Starting with visual thresholds, in the control group the mean t_0 value was 25 ms in both visual fields (*SD* = 12 ms in both cases). The lateralization index between each individual's t_0 values was on average 0.50 (*SD* = 0.08), indicating highly symmetrical thresholds. In the group of patients with large cortico-subcortical lesions, $t_{0\text{left}}$ was on average 34 ms (*SD* = 21 ms), $t_{0\text{right}}$ was 28 ms (*SD* = 12 ms), and the lateralization index was 0.52 (*SD* = 0.08). Neither of these results differed significantly from the mean values in the control group. Most patients in the large lesion group had symmetrical thresholds at normal levels, though three patients had clearly elevated thresholds in the left side. In the basal ganglia group thresholds were close to identical to the control group: $t_{0\text{left}}$ was on average 25 ms, and $t_{0\text{right}}$ was 23 ms (*SD* = 7 ms and *SD* = 10 ms, respectively). No patient deviated from this normal pattern. Also the thalamus patients had thresholds that were close to symmetrical, and at normal levels: on average 27 and 26 ms in the left and right visual fields, respectively. In the group with focal cortical lesions only one patient had an elevated threshold in the left visual field. In summary, all patients but four had symmetrical thresholds at normal levels.

Table 2: Whole Report Estimates

Subject	t_{0left}	t_{0right}	K	C_{left}	C_{right}	C_{index}
Control group						
C1	15 (0.6)	20 (0.5)	3.07 (0.05)	16.3 (1.0)	14.1 (0.8)	0.54 (0.018) >
C2	15 (0.1)	15 (0.5)	4.39 (0.15)	23.1 (1.1)	26.0 (1.2)	0.47 (0.015)
C3	15 (0.0)	15 (0.2)	3.20 (0.08)	19.4 (1.0)	23.1 (1.3)	0.46 (0.017) <
C4	27 (2.4)	27 (2.0)	3.05 (0.04)	14.0 (1.0)	20.8 (1.5)	0.40 (0.017) <
C5	15 (0.0)	15 (0.0)	3.54 (0.08)	24.1 (1.4)	26.6 (1.7)	0.48 (0.020)
C6	50 (8.1)	26 (4.7)	2.56 (0.08)	12.0 (1.4)	11.7 (1.1)	0.51 (0.033)
C7	15 (0.0)	15 (2.9)	3.03 (0.03)	19.5 (1.2)	19.6 (1.3)	0.50 (0.020)
C8	30 (0.8)	24 (3.9)	4.10 (0.08)	26.8 (1.5)	24.7 (1.6)	0.52 (0.019)
C9	37 (14.5)	60 (8.7)	3.32 (0.19)	9.8 (1.7)	13.4 (1.7)	0.42 (0.037) <
C10	31 (8.5)	23 (6.1)	3.07 (0.04)	16.5 (1.8)	20.3 (1.8)	0.45 (0.027)
C11	30 (0.0)	30 (0.0)	3.18 (0.07)	19.4 (1.2)	24.2 (1.7)	0.45 (0.020) <
C12	15 (3.3)	28 (2.3)	3.33 (0.08)	16.1 (1.1)	24.9 (1.6)	0.39 (0.020) <
Large lesion group						
L1	15 (1.1)	15 (1.8)	3.22 (0.06)	18.1 (1.3)	29.1 (2.2)	0.38 (0.023) <
L2	15 (0.1)	15 (2.3)	2.30 (0.07)	8.2 (0.8)	13.0 (1.2)	0.39 (0.027) <
L3	36 (5.1)	40 (0.5)	4.22 (0.19)	15.4 (1.3)	25.7 (1.5)	0.37 (0.020) <
L4	18 (5.3)	24 (4.0)	3.38 (0.13)	9.9 (0.6)	15.6 (1.2)	0.39 (0.023) <
L5	60 (8.4)	30 (5.4)	3.33 (0.11)	11.3 (1.4)	15.2 (1.5)	0.43 (0.029) <
L6	74 (10.6)	30 (6.9)	3.10 (0.07)	6.4 (0.9)	9.4 (1.2)	0.41 (0.034) <
L7	31 (8.7)	33 (6.9)	2.12 (0.05)	7.9 (1.0)	19.9 (2.7)	0.29 (0.029) <
L8	15 (0.1)	15 (0.3)	3.20 (0.05)	18.4 (1.3)	32.6 (2.5)	0.36 (0.022) <
L9	28 (4.5)	23 (3.4)	3.18 (0.05)	23.0 (2.0)	27.1 (2.2)	0.46 (0.025)
L10	30 (3.0)	28 (7.9)	3.20 (0.09)	9.9 (0.9)	15.9 (2.0)	0.38 (0.026) <
L11	15 (0.2)	15 (0.2)	3.23 (0.14)	10.4 (0.7)	17.2 (1.1)	0.38 (0.018) <
L12	75 (7.8)	56 (10.1)	3.43 (0.10)	16.1 (2.2)	21.9 (3.2)	0.42 (0.038) <
L13	22 (7.9)	28 (7.6)	2.15 (0.07)	6.6 (0.6)	8.9 (0.9)	0.42 (0.032) <
L14	40 (7.7)	45 (8.0)	1.15 (0.03)	6.1 (1.3)	14.7 (2.5)	0.29 (0.044) <
Basal ganglia group						
B1	15 (0.7)	15 (3.6)	2.16 (0.05)	12.2 (1.2)	16.2 (1.5)	0.43 (0.028) <
B2	30 (2.9)	35 (7.3)	3.09 (0.06)	15.3 (1.1)	17.5 (1.7)	0.47 (0.025)
B3	28 (1.1)	28 (0.0)	4.26 (0.13)	20.0 (0.9)	32.4 (1.6)	0.38 (0.014) <
B4	27 (2.5)	15 (5.3)	2.10 (0.04)	10.5 (0.8)	17.2 (1.9)	0.38 (0.028) <
Thalamus group						
T1	37 (6.3)	33 (3.8)	3.16 (0.06)	18.0 (1.9)	21.0 (1.8)	0.46 (0.029)
T2	24 (7.0)	27 (3.7)	3.21 (0.08)	13.1 (1.3)	15.2 (1.2)	0.46 (0.026)
T3	30 (4.4)	30 (1.4)	2.26 (0.06)	16.8 (1.7)	17.8 (1.7)	0.49 (0.028)
T4	15 (4.7)	15 (0.6)	2.04 (0.03)	7.2 (0.6)	6.7 (0.6)	0.52 (0.028)
Focal cortical group						
FC1	53 (12.2)	26 (6.9)	1.50 (0.07)	9.6 (2.1)	10.5 (1.8)	0.48 (0.055)
FC2	30 (3.6)	20 (9.9)	2.58 (0.10)	8.9 (1.6)	10.0 (1.7)	0.47 (0.047)
FC3	15 (4.3)	15 (3.5)	2.42 (0.06)	18.6 (2.0)	16.8 (1.6)	0.52 (0.031)

Bootstrap estimates of the standard error of measurement are indicated in brackets.
<: the 95% confidence interval of C_{index} lies below 0.50.
>: the 95% confidence interval of C_{index} lies above 0.50.

Turning to visual processing speed, the average C_{left} value in the control group was 18.1 letters / s (SD = 5.0 s^{-1}) and the mean C_{right} value was 20.8 letters / s (SD = 5.2 s^{-1}). The average lateralization index for C was 0.46 (SD = 0.05). Using bootstrap analysis to take measurement error into account, 5 of the 12 control participants had C_{index} values that were significantly below 0.50, and one participant had a value that was significantly above 0.50. In the large lesion group the average C_{left} value was much lower than in the control group: 12.0 s^{-1} (SD = 5.3 s^{-1}) but the mean C_{right} value was close to normal: 19.0 s^{-1} (SD = 7.3 s^{-1}). Corresponding to this, the C values of patients with large lesions were more asymmetrical than in the control group: The lateralization index for C was on average 0.38 (SD = 0.05), a highly significant deviation from the control group mean of 0.46 ($p < 0.001$, Mann-Whitney). Thus, the asymmetry was markedly stronger than in the control group, with C values about 60% higher in the right visual field compared to about 15% higher for the controls. This side difference was extremely common: 13 out of 14 patients had a C_{index} value that was significantly below 0.50. A similar pattern was found in the basal ganglia group, where the average lateralization index for C was 0.41 (SD = 0.04), a value that was significantly different from the control group mean if a one-tailed test is allowed ($p < 0.05$, Mann-Whitney). Three of the four basal ganglia patients had C_{index} values significantly below 0.50. See Figure 3 for the C_{index} values in the combined basal ganglia and large lesion groups versus the control group. In the thalamic group none of the four patients had any notable asymmetry, and also in the group with focal cortical lesions C values were symmetrically distributed for all three patients. To sum up, asymmetrical processing speed was a highly frequent finding among patients with large lesions and selective damage in the basal ganglia, but the asymmetry did not occur after thalamic or focal cortical lesions.

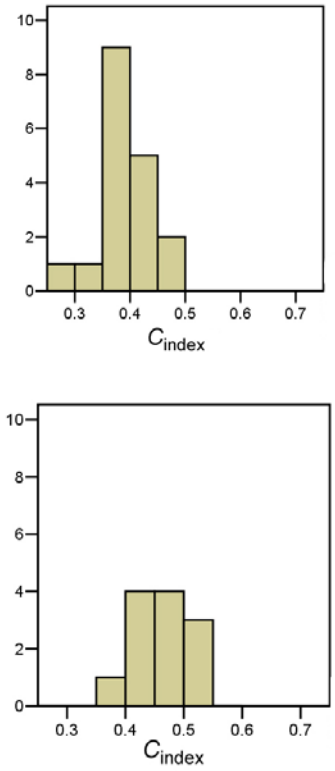

Figure 3. *Distribution of C_{index} values in patients with focal basal ganglia or large lesions (above; n = 18) and in the control group (below; n = 12).*

Regarding the storage capacity of VSTM, the average *K* value in the control group was 3.32 (*SD* = 0.50), consistent with previous findings in healthy subjects (Sperling, 1967; Vogel, Woodman, & Luck, 2001). In the large lesion group, the mean *K* value was 2.94 (*SD* = 0.76). The difference to the control mean was not significant. However there was a clear split in the group: 10 patients had normal *K* values, but four patients had *K* values in the range of 1.15 - 2.30, between two and four *SD*s below the control mean. There was also a mixed picture in the three groups with focal lesions. In the basal ganglia group two out of four patients had markedly reduced *K* values, which was also the case in the thalamus group, and among patients with focal cortical lesions a single patient had a strong reduction of VSTM capacity. *K* seems to be a global parameter

(Duncan et al., 1999) and was estimated across hemifields. As the present article deals with side differences in performance, a detailed discussion of the lesion anatomy of VSTM deficits will be presented in a parallel article (Habekost & Rostrup, in prep). Preliminary analysis suggests that deficits in *K* are linked to either leukoaraiosis or large strokes with substantial white matter involvement.

See Figure 4 for whole report performance pattern of a representative patient in the large lesion group: Approximately equal thresholds, a VSTM limit at normal level, but clearly lower processing speed in the left visual field.

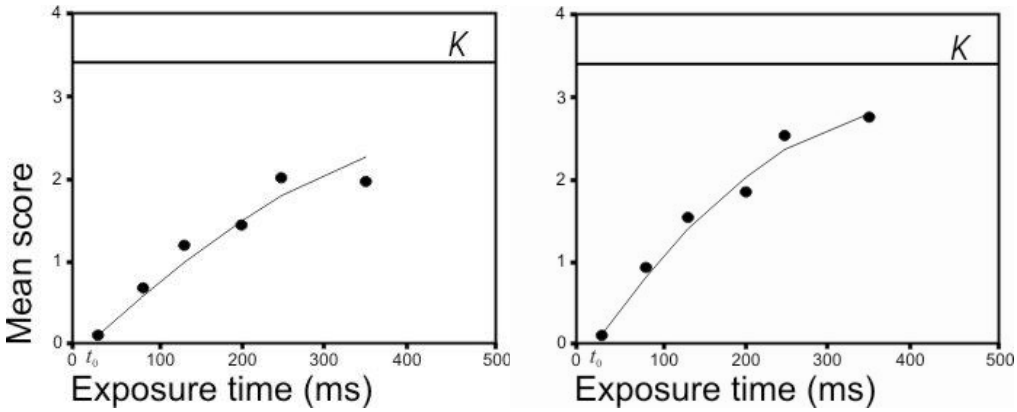

Figure 4. *Whole report performance of a representative patient (L4) with a large lesion. Each panel shows the mean number of correctly reported letters as a function of exposure duration, separately for the left (left panel) and right (right panel) visual fields. Solid curves represent maximum likelihood fits to the observations. The estimate of visual short-term memory capacity, K, is marked by a horizontal line, and t_0 denotes the visual threshold. The slope of the curve at $t = t_0$ corresponds to the visual encoding rate, C.*

3.2. Experiment 2: Partial report

Forming the natural complement of whole report, partial report experiments measure how the total processing capacity is distributed across objects in the visual field. In TVA this corresponds to attentional weighting. Two aspects of weighting are typically investigated: The *task-related* weighting of objects designated as either targets or distractors, and the *spatial* weighting of objects in different parts of the visual field (e.g.,

the weight of objects in the left vs. right hemifield). In partial report experiments only objects belonging to a pre-defined target category (e.g., green letters) are to be reported. Performance in target-only conditions (cf. Figure 1b) is compared with conditions in which both targets and distractors are present (cf. Figure 1c). Score reductions in the distractor conditions reflect the efficiency of top-down attentional control, quantified by the parameter α. In our partial report experiment we included three target-only conditions: Two conditions in which all stimuli occurred in either the left or right hemifield (cf. Figure 1b), and one condition where stimuli occurred in both sides (cf. Figure 1d). The unilateral conditions allowed for estimation of sensory effectiveness separately in each side (quantified by parameter A, which represents the accumulated sensory effect for a fixed exposure duration). In the bilateral condition scores for left and right side stimuli could differ due to reduced sensory effectiveness in one side, but this factor was controlled for by data from the unilateral target-only conditions. Remaining side differences should therefore be attributed to different attentional weighting of each hemifield, which in TVA is quantified by w_{index}. Thus w_{index} represents a pure estimate of spatial attentional bias (controlled for sensory factors) and asymmetries in this parameter correspond closely to the definition of visual extinction.

For a summary of the estimated parameter values from the partial report experiment, along with bootstrap estimates of the measurement errors, see Table 3. Since individual exposure durations were used in the partial report experiment, only intra-individual comparisons between left versus right visual field performance (lateralization indices) are meaningful.

Table 3: Partial Report Estimates

Subject	K'	A_{index}	w_{index}	α_{index}
Control group				
C1	3.17	0.50 (0.027)	0.68 (0.037) >	0.36 (0.064) <
C2	3.12	0.48 (0.018)	0.38 (0.036) <	0.68 (0.106)
C3	4.06	0.43 (0.030) <	0.53 (0.056)	0.38 (0.069)
C4	3.07	0.48 (0.027)	0.41 (0.047)	0.59 (0.072)
C5	4.04	0.46 (0.033)	0.39 (0.052) <	0.39 (0.082)
C6	3.06	0.51 (0.026)	0.63 (0.054) >	0.45 (0.114)
C7	3.03	0.48 (0.024)	0.51 (0.047)	0.46 (0.068)
C8	4.11	0.57 (0.033) >	0.57 (0.075)	0.58 (0.081)
C9	3.04	0.49 (0.033)	0.43 (0.062)	0.55 (0.092)
C10	4.06	0.50 (0.027)	0.66 (0.041) >	0.50 (0.080)
C11	3.14	0.44 (0.028) <	0.78 (0.037) >	0.31 (0.071) <
C12	3.04	0.53 (0.029)	0.44 (0.057)	0.64 (0.090)
Large lesion group				
L1	3.13	0.46 (0.037)	0.27 (0.063) <	0.35 (0.071) <
L2	3.03	0.47 (0.030)	0.21 (0.046) <	0.72 (0.078) >
L3	3.20	0.33 (0.027) <	0.40 (0.060)	0.45 (0.083)
L4	3.17	0.50 (0.030)	0.14 (0.033) <	0.69 (0.093) >
L5	2.33	0.35 (0.039) <	0.33 (0.066) <	0.51 (0.139)
L6	3.06	0.30 (0.025) <	0.15 (0.039) <	0.52 (0.138)
L7	2.36	0.39 (0.038) <	0.12 (0.035) <	0.78 (0.069) >
L8	3.37	0.28 (0.098) <	0.50 (0.152)	0.27 (0.076) <
L9	3.26	0.42 (0.037) <	0.54 (0.055)	0.57 (0.079)
L10	2.73	0.39 (0.041) <	0.15 (0.057) <	0.75 (0.154)
L11	2.43	0.34 (0.040) <	0.35 (0.077)	0.53 (0.080)
L12	3.16	0.44 (0.029) <	0.52 (0.054)	0.54 (0.075)
L13	2.35	0.38 (0.042) <	0.44 (0.066)	0.76 (0.113) >
L14	1.04	0.52 (0.066)	0.34 (0.090)	0.66 (0.126)
Basal ganglia group				
B1	2.03	0.36 (0.026) <	0.10 (0.028) <	0.54 (0.159)
B2	3.13	0.47 (0.021)	0.52 (0.037)	0.51 (0.077)
B3	4.03	0.44 (0.033)	0.47 (0.049)	0.53 (0.081)
B4	2.09	0.39 (0.051) <	0.57 (0.073)	0.58 (0.085)
B5	2.22	0.36 (0.034) <	0.47 (0.056)	0.38 (0.098)
Thalamus group				
T1	3.49	0.42 (0.031) <	0.50 (0.050)	0.43 (0.082)
T2	3.19	0.52 (0.028)	0.51 (0.037)	0.56 (0.081)
T3	2.34	0.51 (0.042)	0.28 (0.047) <	0.51 (0.107)
T4	2.26	0.47 (0.027)	0.49 (0.052)	0.72 (0.107) >
Focal cortical group				
FC1	1.66	0.41 (0.052)	0.37 (0.087)	0.63 (0.136)
FC2	3.13	0.49 (0.032)	0.47 (0.066)	0.58 (0.087)
FC3	3.15	0.51 (0.022)	0.63 (0.043) >	0.52 (0.082)

Bootstrap estimates of the standard error of measurement is indicated in brackets.
<: the 95% confidence interval of A_{index} / w_{index} / α_{index} lies below 0.50.
>: the 95% confidence interval of A_{index} / w_{index} / α_{index} lies above 0.50.

The average A_{index} value in the control group was 0.49 (*SD* = 0.04), and taking measurement error into account the A_{index} values of most controls did not differ reliably from 0.50. In the large lesion group the average lateralization index for *A* was 0.40 (*SD* = 0.07). The difference from the control group's mean lateralization index for *A* was highly significant ($p < 0.005$, Mann-Whitney). According to the bootstrap analysis, 10 of the 14 patients had an A_{index} value significantly below 0.50. In the basal ganglia group the pattern was similar. The mean A_{index} was 0.40 (*SD* = 0.05), again a significant difference ($p < 0.01$, Mann Whitney) from the control mean. Three out of the five patients in this group had an A_{index} value that was significantly below 0.50, and a fourth patient (B3) came very close to this. See Figure 5 for the distribution of A_{index} values in the basal ganglia and large lesion group versus the control group. The results are highly consistent with the findings on C_{index} in whole report. Weaker sensory effectiveness in the left visual field was thus a very consistent characteristic of patients with large lesions or focal basal ganglia damage. However in the focal cortical group A_{index} values were normal for all patients, and in the thalamus group A_{index} differed reliably from 0.50 only for a single patient.

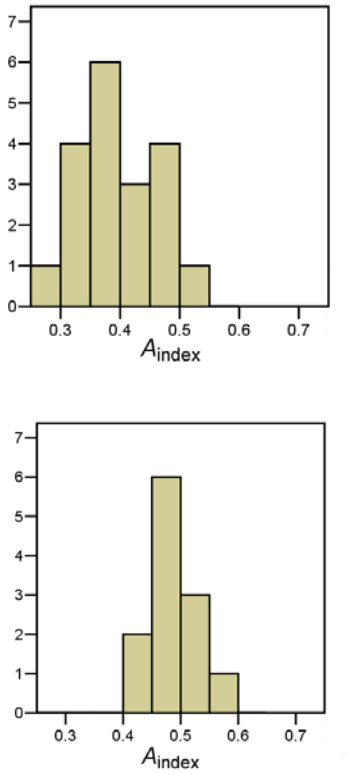

Figure 5. *Distribution of A_{index} values in patients with focal basal ganglia or large lesions (above; n = 19) and in the control group (below; n = 12).*

The average w_{index} value in the control group was 0.53 (*SD* = 0.13). In the large lesion group, the average w_{index} was 0.32 (*SD* = 0.15), reflecting a general extinction tendency in addition to the reduced sensory effectiveness in the left visual field (cf. A_{index}). The difference to the control mean was highly significant ($p < 0.005$, Mann-Whitney). Seven out the 14 patients had an index value significantly below 0.50, with three others (L3, L11, L14) coming close.[6] In the basal ganglia group the average w_{index} was 0.43 (*SD* = 0.19), but only for a single patient was there a reliable bias towards the right visual field. In the focal cortical group w_{index} values were all in the normal range. Three thalamic

[6] The deviations of these three patients would have been significant at a one-tailed test. Another patient (L8) had a "normal" w_{index} estimate of 0.50, which the bootstrap analysis indicated was unreliable. The bootstrap distribution was bimodal, and the standard error of measurement was 0.15, much higher than usual. This variation was probably due to the patient's near-ceiling performance with unilateral right visual field stimuli, which made estimation of *A* values in this side unreliable, and thus indirectly confounded the w_{index}.

patients also had values very close to 0.50, but one patient in this group had an extinction-like pattern. In sum, asymmetries in attentional weighting were specific to patients with large lesions, except for a single basal ganglia and a single thalamic patient. See Figure 6 for the distributions of w_{index} values in the large lesion and control groups, respectively.

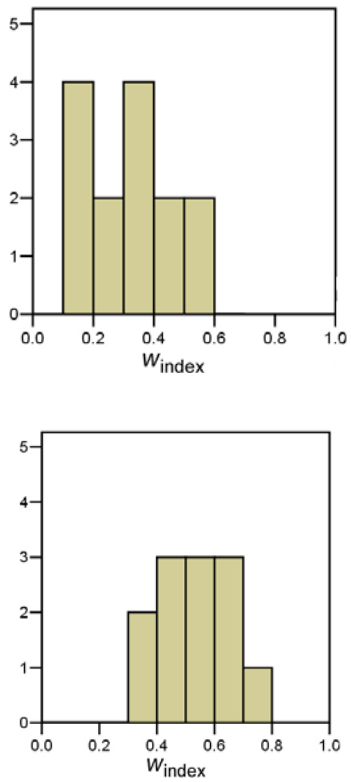

Figure 6. *Distribution of w_{index} values in patients with large lesions (above; n = 14) and controls (below; n = 12).*

The average α_{index} value was 0.49 (*SD* = 0.12) in the control group, indicating that visual selectivity was on average symmetrical. The corresponding values were 0.58 (*SD* = 0.16) in the large lesion group and 0.51 (*SD* = 0.07) in the basal ganglia group. The difference to the control mean was not significant in either group, although it came close in the large lesion group (p = 0.07, one-tailed Mann-Whitney). In both the thalamus and focal cortical groups, the mean α_{index} was higher than normal (0.56 and 0.57, respectively),

but both findings failed to reach significance. Looking at intra-individual differences, in the large lesion group each patient's α_{left} value was close to significantly higher than the α_{right} value ($p = 0.06$, one-tailed Wilcoxon Signed ranks), and the side difference reached significance in the patient group as a whole ($p < 0.05$, two-tailed Wilcoxon signed ranks). Thus there was a general trend towards higher (i.e., poorer) α values in the left visual field for patients. However there was considerable inter-individual variability in the α estimates of both controls and patients, which reduced statistical power to show effects in specific patient groups or individuals. This reflects the fact that α estimates were related to much higher measurement error than the other TVA parameters (cf. Table 3). This was also found by Habekost and Bundesen (2003), and there are mathematical reasons to expect estimation of α parameters to be vulnerable to noise in the data (due to α being a ratio of parameters). Given this limitation in statistical power the data only allow the general conclusion that left-side reductions of top-down selectivity were more frequent among patients than controls. One potential confound should also be addressed: Besides asymmetrical top-down selectivity, the asymmetry in α values could be due to different efficiency of colour perception (a necessary condition for selection of targets) in the two hemifields. This possibility was investigated in the colour report experiment.

3.3. Experiment 3: Colour report

The colour report experiment was a forced-choice naming task, and the following analysis is based on mean scores after correction for guessing. Surprisingly, colour report was significantly better in the left visual field for controls: The average number of correctly reported colours in the left and right side was 4.09 and 3.69, respectively ($p < 0.05$, Wilcoxon signed ranks). However in the patient group there was no

significant side difference in scores (left visual field: 3.39 vs. right visual field: 3.44, ns), nor were there significant differences in any of the subgroups. Thus side differences in colour perception cannot account for the asymmetry in α values described above.

3.4. Lesion anatomy and test performance

Three patients had markedly higher perception thresholds in the left visual field, and one patient had high thresholds in both sides. Three of these patients had large lesions, whereas the fourth had a small lesion in the posterior parietal cortex. There was no significant correlation between lesion size and $t_{0\text{index}}$ in the patient group as a whole (n = 23; r_s =-0.05, ns), nor in the large lesion group alone (n = 13; r_s = -0.25, ns). Also, there was no common area in which the three patients with large lesions were damaged, but other patients with normal thresholds were not. Thus threshold abnormalities were sporadic and not systematically related to either lesion volume or a particular location.

A much more robust finding was that C values were close to uniformly reduced in the left visual field after both large cortico-subcortical and focal basal ganglia lesions: The C_{index} was generally about 0.40 in these groups. No significant correlation between lesion volume and C_{index} was found in the two groups combined (n = 17; r_s = -0.29, ns), nor in the large lesion group alone (n = 13; r_s = -0.03, ns). In these two patient groups there was a strong common damage focus around the putamen and adjacent white matter (see Figure 7 for a lesion density plot). In all 17 patients but one, this area was affected. The lesions generally seemed to fan out from this area and involved other areas, especially the “remote” posterior cortical, to a variable degree.

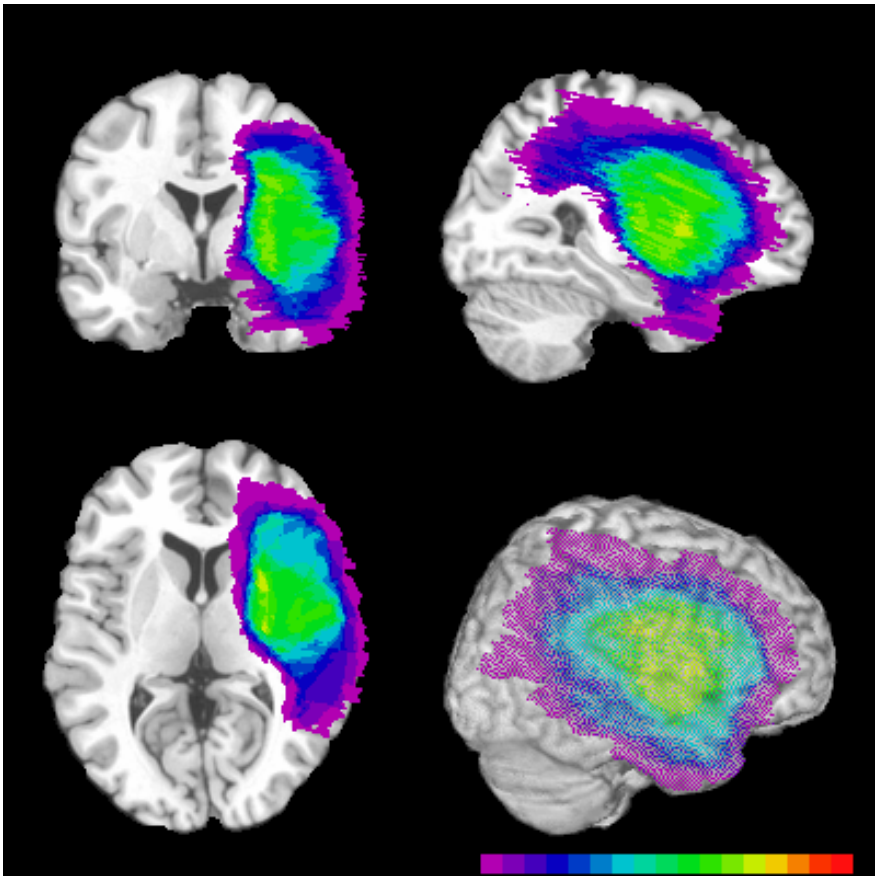

Figure 7. *Density plot of normalized lesions for patients in the large lesion and basal ganglia groups (n = 17; no MR scans were available for two additional patients). The number of overlapping lesions is illustrated by different colours coding increasing frequencies from violet (n = 1) to red (n = 17).*

For a stringent test of critical areas for C_{index}, we performed a voxelwise test across the normalized MR scans of all patients (see Figure 8). The test revealed a focal area in the right putamen and surrounding white matter where damage was significantly related to low C_{index} values. Significance values peaked in the posterior putamen, whereas parts of the insula were less strongly related to C_{index}. In summary, a focal lesion in the putamen region was sufficient to reduce C in the left visual field to about two-thirds of the right visual field value, but additional damage (even very extensive) did not add further to this asymmetry.

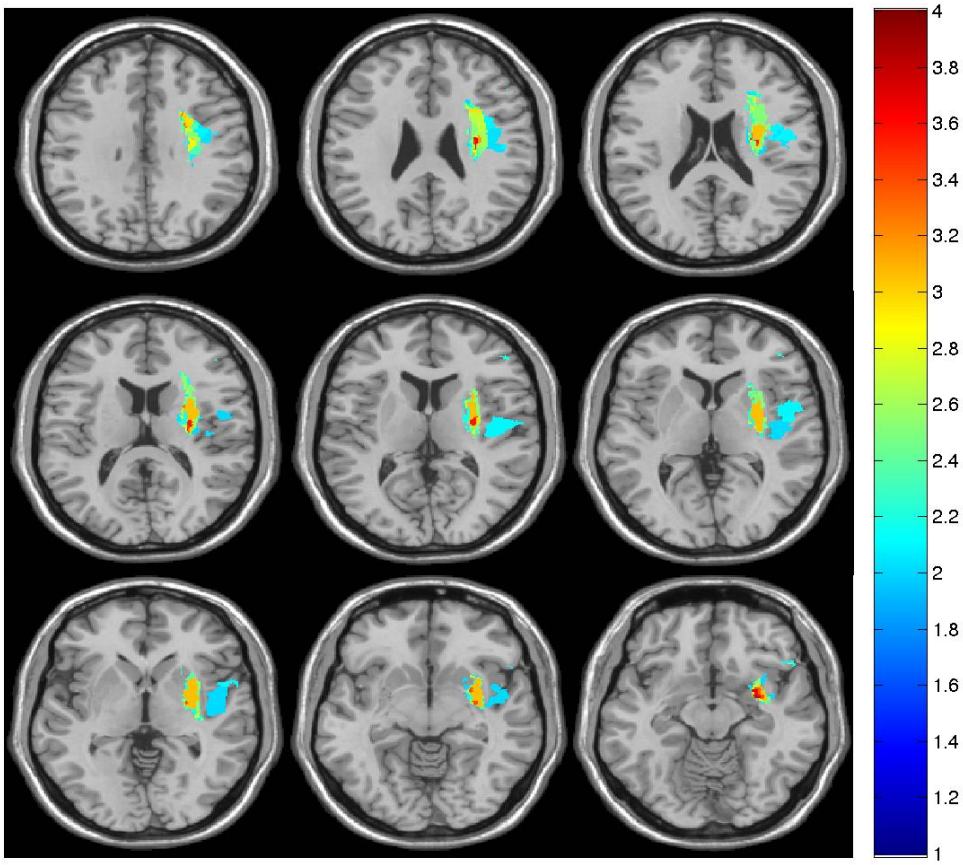

Figure 8. Voxelwise statistical test of critical areas for C_{index}. Each brain voxel is colour coded according to the value of -log_{10}(p), ranging from a significance level of p = 0.1 (dark blue) to p = 0.0001 (dark red).

The importance of posterior cortical areas, in particular the parietal lobe, was less clear. Most patients (eight patients in the large lesion group, and by definition all patients in the basal ganglia group) had either no or very little affection of the parietal lobe. Of four patients with selective injuries in the posterior cortex, only one had a C_{index} value similar to patients with lesions involving the putamen. This patient's lesion was much larger than the other three and involved most of the posterior parietal cortex. Regarding the four thalamic patients, none had asymmetries in *C*.

Concerning A_{index}, a closely related parameter to C_{index}, findings were similar: Performance in the right visual field was generally about 50% better in both the large lesion and basal ganglia group, but symmetrical in the other groups. The asymmetry of A values was related to the same pattern of lesions as $C_{index.}$

Another main finding was the frequent occurrence in the large lesion group of low attentional weighting of the left side. In the patient group as a whole, the correlation between lesion volume and w_{index} was significant (n = 23; r_s = -0.40, one-tailed $p < 0.05$), but within the large lesion group volume was clearly irrelevant (n = 13; r_s = -0.06, ns). In other words low attentional weighting of the left side was related to large lesions, but above a certain size, volume differences did not matter. Visual extinction is traditionally related to lesions in the posterior parietal lobe (e.g., Posner, Walker, Friedrich, & Rafal, 1984; Milner & Goodale, 1995), and has recently been linked to the temporo-parietal junction (Karnath et al., 2003). However, most patients in the large lesion group had minimal or no involvement of these areas. Lesions were typically more anterior, and involved subcortical structures to a higher extent than posterior cortical areas (cf. Figure 7). Of the three patients who did not have a clear tendency towards asymmetrical weighting, one had a lesion that covered most of the posterior parietal lobe and another also had considerable parietal damage. The present data do not allow us to evaluate the relation between parietal lesions and extinction, but instead point to a different type of stroke. The results show that attentional weighting was generally asymmetric after large strokes in the anterior part of the territory of the middle cerebral artery that involved several cortical and subcortical structures.

Besides patients with large strokes, two patients with focal lesions had asymmetric attentional weighting. The first of these patients (T3) had a thalamic lesion,

which can be directly compared with the lesions of three other thalamic patients who had symmetric attentional weighting. Consider the subtraction of patient T3's normalized lesion from the combined lesions of these other patients (see Figure 9). The subtraction revealed a unique area of damage in this patient: the anterior lateral part of the pulvinar nucleus. Contrary, the lesions of the three other patients were all located anterior to the posterior commissure, a landmark for the anterior border of the pulvinar (Talairach & Tournoux, 1988). The importance of the pulvinar is closely in line with predictions about the location of a "map of attentional weights" in the neural TVA theory (Bundesen et al., in press). There is no similar theoretical explanation for the weighting asymmetry of the second patient (B1), who had a lesion in the most posterior part of the putamen and a small part of the corona radiata. However MRI cannot reveal all effects of brain damage, and subcortical lesions may sometimes, due to their connectivity pattern, profoundly affect the function of larger, structurally intact parts of the brain (Vallar, Cappa, & Wallesch, 1992).

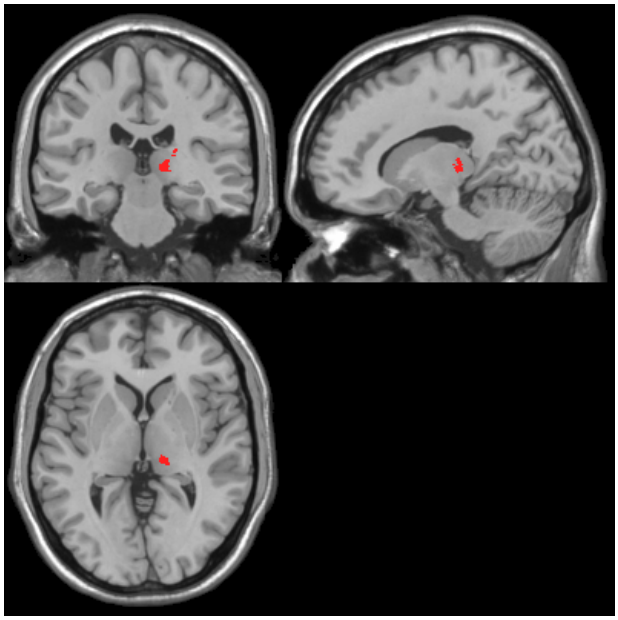

Figure 9. *The thalamic area uniquely damaged (shown in red) in a patient (T3) with asymmetrical attentional weighting, based on subtraction of lesions of three other thalamic patients with normal attentional weighing.*

Turning to top-down selectivity there was a general, though not very strong, trend towards impaired performance in the left visual field for the patients. The correlation between this asymmetry (i.e., α_{index}) and lesion volume did not reach significance (r_s = 0.28, ns), although by a parametric test it came close (r = 0.33, one-tailed p = 0.06). As explained in section 3.2, statistical power was relatively low in the estimation of α, and we think it is plausible that a relation between α asymmetry and lesion volume could have been demonstrated in a larger patient group.

4. Discussion

We measured a range of visual parameters, sensory and attentional, in twenty-six patients with stroke in the right side of the brain. The test results were compared to MRI scans of each patient. In spite of the fact that patients were in the stable phase of recovery and had only minor or no clinical deficits, visual asymmetry was a common finding. We found two main types of deficit, one related to perception of unilateral displays, the other occurring with bilateral stimulation. In the following we discuss how these deficits were related to the underlying lesion anatomy.

4.1. Visual thresholds

Only three patients had clearly higher thresholds in the contralesional side. Neither of these patients had lesions that differed in obvious ways from other patients, both when comparing lesion location and volume. Besides the generally symmetric thresholds it is interesting to note that most patients had thresholds at the same level as in the control group: 15 – 30 ms. One explanation for these results is that t_0 – the minimum

exposure time needed for visual identification – depends primarily on bottom-up input to early visual areas. The patients in this study all had damage in areas further downstream in visual processing (temporal or parietal cortex and beyond) which provide top-down modulation of the activity in primary visual areas. It is possible that changes in this top-down input modulates the efficiency of visual processing (as reflected in the encoding speed, *C*, see next section), but in most cases cannot completely erase a signal that carries above-zero information (i.e., change the threshold).

4.2. Visual processing speed

The patients in the large lesion and basal ganglia groups had a quite uniform reduction of visual processing speed in the left visual field: both the C_{index} and A_{index} were generally about 0.40. Regardless of lesion size, almost all these patients had damage in a subcortical area that encompassed the putamen and adjacent white matter, and to a lesser extent the insula (large lesions only). The lesions of many patients also included large cortical regions, but this did not lead to further reductions in contralateral processing speed. A voxelwise statistical analysis showed that damage in the putamen area was significantly related to deficits in contralateral visual processing speed. On theoretical grounds both the putamen itself and the adjacent white matter could be relevant. The putamen is traditionally associated with motor function. For example, in primates the posterior and middle putamen is somatotopically related to arm and face movements (Alexander & Cruther, 1990). Given this, it may not seem obvious that the putamen is involved in visual processes. However several recent studies have linked the putamen with visual attention. Functional imaging studies have found activation of the putamen in tasks involving shifts of visuo-spatial attention (Gitelman et al., 1999; Kim et al., 1999). Also

lesion studies have pointed to putaminal involvement in visual attention. Karnath et al. (2002, 2004) found that the putamen was one of a few subcortical structures critical for neglect, and Fimm et al. (2001) showed that (right) putamen lesions can lead to deficits in visual search. These studies generally support the notion that the putamen is part of a large anatomical network responsible for orienting attention in space (Mesulam, 2000). However a deficit in visual orienting, implying a combination of motor and perceptual components, cannot explain the present results. Stimuli were presented within a single fixation, which ruled out eye movements, and there was no significant motor component in the response (unspeeded verbal report). The result can be interpreted according to theories that criticize the traditional strong division between perceptual and motor function (Allport, 1987; Hommel, Müsseler, Aschersleben & Prinz, 2001; Neumann, 1987). Assuming a network organization of sensorimotor systems where functionally connected areas exert strong reciprocal influence on each other, it is plausible that damage in a "motor" area involved in visual orienting also lead to subtle disturbances in a purely perceptual task.

The affection of white matter may also be relevant. Fimm et al. (2001) found a lateral bias in visual search following subcortical lesions, and hypothesized that damage in the posterior limb of the internal capsule leads to disconnection of central nodes in a posterior network for attentional orienting (Posner & Petersen, 1990): the posterior parietal cortex and the thalamus. Another possibility, qua the discussion above, is that a unilateral impairment of motor functions mediated by the internal capsule also leads to subtle disturbances in the visual system.

Though damage in structures outside the putamen area did not lead to additional asymmetry in visual processing speed, it is very unlikely that the cortex is

irrelevant to the deficit. Visual neglect has been related to lesions in the insula (Manes, Paradiso, Springer, Lamberty, & Robinson, 1999), the inferior frontal lobe (Husain & Kennard, 1996), the superior temporal gyrus (Karnath et al., 2001, 2004) and the inferior parietal lobe (Vallar & Perani, 1986; Mort et al., 2003). Also, fMRI studies point to a network for exogenous orienting of visual attention with central nodes in the temporo-parietal junction and the inferior frontal gyrus (Corbetta, Kincade, & Shulman, 2002). The importance of these cortical areas for the C_{index} and A_{index} was probably occluded by two factors in our study: (a) only few patients had damage in these regions without involvement of the putamen area also. A single patient with a large, selective parietal lesion did have an asymmetry of *C* values, but the deficit was not found with small posterior cortical lesions. However, other TVA studies have found asymmetry of sensory effectiveness after more focal lesions in the right parietal cortex (Duncan et al., 1999; Peers et al., in press). More interesting, (b) there seemed to be a floor effect in the experiments such that visual perception of unilateral stimuli could be impaired only to a certain degree, even after very large lesions. Unlike the w_{index}, the C_{index} and A_{index} rarely fell much below 0.40. In other words top-down facilitation of visual processing from the parietal, frontal and insular cortices, as well as the putamen area, only seemed to account for a limited part of the perceptual efficiency with unilateral displays. Once top-down facilitation was impaired, even after small lesions in the putamen or white matter, visual function seemed to rely on processing of the bottom-up signal to early visual areas and transmission to the left hemisphere for further analysis. However this was only possible if the left hemisphere was not simultaneously engaged in processing stimuli from its "own" right visual field. In that case, left visual field stimuli were often missed ("extinguished").

4.3. Determinants of visual extinction

Several models for visual extinction have been proposed (for an overview see Heilman et al., 2003). A historically central discussion concerns the involvement of sensory versus attentional factors in the phenomenon (Bender, 1952; di Pellegrino & De Renzi, 1995; Vallar et al., 1994). In addition, it is often assumed that extinction patients have reduced general attentional capacity (Mattingley, 2002). The present study is very relevant to these topics, since it includes separate estimation of sensory, attentional, and general capacity measures for each patient. We discuss our findings in the context of a model developed by Marzi et al. (2001), which is explicit about the influence of both sensory effectiveness and general capacity on visual extinction. Marzi et al.'s model was designed to account for extinction in simple detection tests such as the clinical confrontation method. They suggested that stimuli compete for access to a decision center in the left hemisphere making numerosity judgements (e.g., were one or two stimuli presented?). After damage to the right side of the brain, two factors give left visual field stimuli a disadvantage in the race towards the decision center. The first is an intra-hemispheric lack of top-down signals, which leads to slower processing of contralesional items even when these are shown in isolation (cf. our findings on C and A values). The second factor is an inter-hemispheric impairment of callosal transmission. This leaves right visual field stimuli (that are already represented in the left hemisphere) essentially free from competition from left visual field stimuli that have to be transmitted across the corpus callosum to influence the race. Together these two conditions lead to a relatively weak signal from the contralesional field, an impairment that only has slight effects with unilateral stimulation, but causes the left visual field signal to be wiped out in case of bilateral stimulation (i.e., extinction). The findings of the present study are compatible

with both these assumptions. Perception of letters have been linked to the left extrastriate cortex (Flowers et al., 2004; Polk et al., 2002), and because our experiments required identification of alphabetic stimuli, it is reasonable to assume that encoding into VSTM should depend on activity in the left hemisphere. Corresponding to Marzi et al.'s first factor, the *C* values for contralesional stimuli were reduced in most patients. Following the discussion in the preceding section, this was probably due to weaker top-down signals to primary visual areas in the right side of the brain. However the reduction in *C* and *A* values did not in itself lead to extinction (i.e., a strong asymmetry of attentional weighting). Extinction-like performance was found only for patients with large cortico-subcortical lesions (or in a single case, pulvinar damage), whereas basal ganglia patients, who also had reduced *C* and *A* values, generally did not show extinction effects. A second factor seemed necessary, which could be a marked weakening of callosal transmission from the right hemisphere following large lesions.

Marzi et al. also argued that a third factor is necessary for extinction: an impairment of general attentional capacity. Otherwise the left visual field stimulus should eventually reach the decision center (and thus, consciousness) although it would usually be preceded by the stronger right side signal. However, most patients in our study had intact VSTM capacity. Thus a strong asymmetry of attentional weighting can also be found in patients with normal capacity, if only the stimulus display is so complex that items in the ipsilesional field can potentially fill up VSTM ("multi-item extinction*"*).

In summary, our results suggest that for extinction to occur in the chronic phase (in tasks that require the eventual involvement of the left hemisphere) it generally takes a large right side lesion, presumably leading to impaired callosal transmission from this hemisphere. Such lesions typically also cause reduced sensory effectiveness for left

visual field stimuli, but this deficit is not in itself sufficient to cause extinction. Extinction may also occur in pure form (i.e., with preserved sensory effectiveness) after selective pulvinar damage. A reduction of attentional capacity may be necessary for extinction to occur in simple two-stimulus detection tasks, but if the display is sufficiently complex extinction effects can also be found in patients with normal attentional capacity.

4.4. The neural basis of visual extinction

Like visual neglect (Mort et al., 2003; Vallar & Perani, 1986) extinction is traditionally related to posterior parietal lobe lesions (Critchley, 1949; Milner & Goodale, 1995; Posner et al., 1984). A different view has recently been proposed by Karnath et al. (2003) who point to the temporo-parietal junction as the critical area. However the asymmetries we found in w_{index} were not related to damage in either of these cortical regions. Lesions above a certain size in the territory of the middle cerebral artery, especially frontal and basal ganglia areas, in general caused lower attentional weighting of the left visual field. The present results agree better with the alternative suggestion that extinction can follow a much broader distribution of lesions (Vallar et al., 1994). This view lends theoretical support from the biased competition theory of attention (Desimone & Duncan, 1995), which predicts unbalanced attentional weighting ("competition") as a very general consequence of unilateral brain injury (Duncan, 1999). Consistent with this, a recent TVA investigation of patients with focal damage in either the parietal or frontal cortex found that spatial bias was correlated to simple lesion volume (Peers et al., in press). Also in the present study, small lesions did in general not lead to asymmetrical weighting. Thus the strength balance between the two hemispheres seems fairly robust,

and to disturb the equilibrium it may require a unilateral lesion of a considerable size in the cerebral network for vision.

One exception to this rule may be lesions in the pulvinar nucleus of the thalamus. Of the four patients with thalamic lesions in this study, only the one (T3) with damage in this structure had clearly lower attentional weighting of the left visual field (cf. Figure 8). The finding is consistent with single cell, lesion and imaging studies (reviewed in Bundesen et al., in press) which point to the pulvinar as a likely site for a "map of attentional weights" in the contralateral visual field. However the present finding is based on only a single case, and it should also be noted that one of the twelve control participants (C11) had an even more asymmetrical weighting pattern. Except for the possibility of undetected brain damage in this control participant, the pattern was probably due to peculiar strategic factors in his test approach. It cannot be ruled out that patient T3 also chose to use an abnormal strategy, but it is remarkable that out of twelve patients with small lesions, the only one with a pure (i.e., symmetric sensory effectiveness) weighting bias also happened to be the only one with pulvinar damage. The finding awaits confirmation from studies of more patients.

4.5. Visual selectivity

In a previous TVA study, Duncan et al. (1999) found that top-down selectivity was preserved bilaterally in a group of nine neglect patients. However this study did not include bootstrap analysis of the measurement error related to α estimates. In the present study we found substantial measurement error related to α, which suggests that Duncan et al.'s negative finding may have been caused by low statistical power (the patient group was about three times smaller than in the present study). However the finding may also

reflect the distribution of lesions in Duncan et al.'s study, which was generally more posterior than in our sample of patients. In the present study we found a tendency towards lower top-down selectivity in the left visual field that could not be explained by side differences in colour perception (i.e., target-distractor discriminability). The data did not allow this general tendency to be coupled with particular lesion patterns. A correlation with overall lesion volume fell short of significance, but we suspect this association could be demonstrated in a larger patient group. In a patient study of similar size by Peers et al. (in press), absolute levels of α values (just) reached a significant correlation with lesion volume. Still, besides statistical power, a reason for the limited findings on visual selectivity might be the distribution of lesions in our patient group. Top-down control of visual attention has been related to the superior frontal gyrus (Corbetta et al., 2002; Hopfinger, Buonocore, & Mangun, 2000) and the fronto-median cortex (Weidner, Pollmann, Müller, & von Cramon, 2002), areas which were almost universally preserved in our patient group.

4.6. Prevalence and clinical significance

Previous studies have tended to estimate the chronic prevalence of visual neglect rather low (e.g., Maguire & Ogden, 2002) especially in patients with intact visual fields (Samuelsson et al., 1997), and the frequency of extinction in the stable phase of recovery is unknown. The present study suggests that neglect and extinction as traditionally defined represent only the most extreme visual asymmetries after right side stroke. Our results indicate that more subtle forms of visual asymmetry are very common effects of this type of brain damage, and persist in a more or less chronic form. In particular, stroke in the territory of the middle cerebral artery consistently lead to

asymmetry in our study. Out of 22 patients with this type of stroke, only a few patients with small cortical or anterior putamen infarcts had symmetrical performance with both unilateral and bilateral stimulation. This high prevalence seemed related to a particular vulnerability of the putamen and surrounding white matter to vascular accidents.

However widespread, one may question the clinical relevance of these deficits. After all, most of our patients were not clearly affected on standard tests of visual neglect and extinction. Also, though we could demonstrate by bootstrap analysis that the observed side differences were reliable in each individual case, there was some overlap with the performance of control participants. Some patients reported experiences (often vague) of impaired perception in the left side, and were satisfied to have these impressions confirmed. Yet, many others were surprised when informed of their test results. On the basis of the present results, we cannot say whether the asymmetries had an impact on the daily life of the patients. The fact however remains that for a large majority of our patients, visual processes occurred with lower efficiency for stimuli in the left visual field. The wider consequences, both functional and phenomenological, of these subtle disturbances represent an interesting avenue for future research.

5. Conclusion

This large patient study demonstrated two main types of visual asymmetry after stroke in the right side of the brain. One was related to perception of unilateral displays (parameters C_{index} and A_{index}), the other occurred with bilateral stimulation (parameter w_{index}). Whereas both deficits seem to be highly common effects of (chronic) stroke in the middle cerebral artery, lesion analysis revealed different kinds of critical

damage. A lesion in the putamen and surrounding white matter was sufficient to impair perception of unilateral displays in the left visual field, and the deficit was not exacerbated with additional involvement of large cortical areas. In contrast, under bilateral stimulation an extinction-like bias was common after large strokes but rarely occurred after focal lesions, with the notable exception of a single patient with damage in the pulvinar nucleus. However in general, thalamic or focal cortical damage did not lead to visual asymmetries. Furthermore, and contrary to influential theories of extinction and neglect, neither of the two deficits had any special relation to damage in the parietal or temporal cortex. Concerning a third attentional function tested, visual selectivity (parameter α), there was a general trend towards poorer function in the left visual field, which however could not be related to specific damage patterns.

Corresponding to the findings on lesion anatomy, TVA based analysis of the psychophysical data revealed distinct functional components underlying test performance. Impaired perception of unilateral left side displays was related to lower visual processing speed in this side, whereas visual thresholds and visual short-term memory were generally normal. An exacerbated side difference under bilateral stimulation (extinction effect) was quantified using the concept of attentional weighting, a pure measure in the sense that it is controlled for sensory effects. Measurements of attentional capacity showed that, contrary to standard theory, extinction effects may also occur in patients with normal capacity.

Together these findings represent a set of visual asymmetries that are minor, but widespread after stroke in the territory of the right middle cerebral artery. Importantly, the deficits persist into the stable phase of recovery. The present study describes the cognitive structure and lesion anatomy of this common effect of right side stroke.

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Appendix: TVA theory

The following summary was adapted from Habekost and Bundesen (2003). In TVA, attentional selection of a visual object *x* consists in encoding the object into visual short-term memory (VSTM). Objects in the visual field can be processed in parallel, and the objects that are selected (and, therefore, can be reported) from a briefly exposed visual display are those objects whose encoding processes complete before the sensory representation of the display vanishes and before VSTM has been filled up with other objects. Thus, objects in the visual field compete for encoding into VSTM, and the competition is a race. In normal subjects, the storage capacity of VSTM is limited to *K* objects, where *K* is about 4, so up to 4 objects can be reported from a brief display.

Consider, first, the processing of a stimulus display consisting of a single object *x*. Suppose *x* is displayed for *t* ms and immediately followed by a mask. In TVA, the time taken to encode *x* into VSTM is exponentially distributed. Specifically, the probability that object *x* gets encoded into VSTM equals

$$P_x = 1 - \exp\left[-v_x * (t - t_0)\right]. \qquad (1)$$

In Equation 1, t_0 denotes the *minimal effective exposure duration*, below which information uptake from the display is assumed to be zero, and the equation presupposes that $t \geq t_0$. Typical estimates for t_0 in young healthy subjects are about 20 ms. The difference $(t - t_0)$ is the *effective exposure duration* of the stimulus display; if the stimulus presentation had been unmasked, an additional effective exposure duration of μ ms should have been added to $(t - t_0)$. The rate parameter v_x can be described as the "speed" at which

element *x* races toward VSTM. At $t = t_0$, v_x is the slope of the function relating the report probability P_x to the exposure duration *t*. When *x* is the only object in the visual field, v_x equals the *sensory effectiveness* of object *x*, s_x. The sensory effectiveness of an object depends on such factors as stimulus discriminability, contrast, and retinal eccentricity.

Both sensory effectiveness, s_x, and minimal effective exposure duration, t_0, can be estimated from a curve showing how report probability P_x increases as a function of exposure duration *t* when object *x* is presented alone. The product of s_x and $(t - t_0)$ is the *accumulated sensory effect* (A_x) of object *x* at time *t*,

$$A_x = s_x * (t - t_0). \quad (2)$$

Some experimental designs, such as the partial report experiment in the present study, provide estimates for A_x without providing separate estimates for s_x and t_0. In such cases, A_x may be taken as an indirect measure of sensory effectiveness if the effective exposure duration is kept constant.

Consider, next, the processing of a display consisting of multiple stimuli. In this case the processing rate of object *x* (v_x) depends not only on the sensory effectiveness of object *x* (s_x) but also on the relative attentional weight of object *x* ($w_x / \Sigma_{z \in S} w_z$):

$$v_x = s_x * (w_x / \Sigma_{z \in S} w_z). \quad (3)$$

As *S* denotes the set of all objects in the visual field, the relative attentional weight of object *x* is the attentional weight of *x* (w_x) divided by the sum of the attentional weights across all objects in the visual field ($\Sigma_{z \in S} w_z$).

In TVA, the processing capacity, *C*, for any given display is defined as the sum of all *v* values in the display:

$$C = \Sigma_{z \in S} v_z. \quad (4)$$

Thus, *C* is a measure of the total rate of information uptake (in objects per second). For displays consisting of objects with the same sensory effectiveness, s_x, Equations 3 and 4 imply that *C* is constant across variations in both the number of objects in the display and their attentional weights. Thus, when sensory effectiveness is kept constant, *C* may be regarded as a fixed total processing capacity divided among the different objects in the display, and the weight ratio $w_x / \Sigma_{z \in S} w_z$ may be regarded as that proportion of the total processing capacity *C* that is allocated to element *x*. When sensory effectiveness varies between objects in different parts of the visual field, separate estimates of processing capacity *C* may be obtained for different parts of the visual field (e.g., for the left vs. the right visual hemifield). This procedure was used in our whole report experiment.

In some tasks (e.g., partial report), the subject is required to focus on target objects but ignore distractors. In order to perform such tasks efficiently, the attentional weights for targets should be higher than for distractors. The ratio (α) between the weight of a distractor ($w_{distractor}$) and the weight of a target (w_{target}) is a measure of the efficiency of selection:

$$\alpha = w_{\text{distractor}} / w_{\text{target}}. \quad (5)$$

An α value of 1 represents nonselective processing, whereas a value of 0 indicates perfect selection. If distractor and target weights are pooled across all positions, an α estimate pertaining to the whole display can be obtained. However, as with C, parameter α can also be estimated in separate parts of the visual field, if the pooling of weights is done over only the region in question.

In other contexts it is relevant to compare the attentional weights of (target) objects in different parts of space. This can be done by computing a relative index (w_{index}) for attentional weights. For example in case of left versus right side comparisons:

$$w_{\text{index}} = w_{\text{left}} / (w_{\text{left}} + w_{\text{right}}) \quad (6)$$

where w_{left} is the attentional weight of a target in the left visual field, and w_{right} the weight of a right side target.

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VISUAL ATTENTION CAPACITY AND WHITE MATTER DAMAGE

Thomas Habekost

Center for Visual Cognition, Department of Psychology, University of Copenhagen

Egill Rostrup

Danish Research Centre for Magnetic Resonance, Hvidovre Hospital, Copenhagen

Abstract

Recently there has been a growing interest in visual short-term memory (VSTM) including the neural basis of the function. Processing speed, another main aspect of visual attention capacity, has received less investigation. For both functions, human lesion studies are sparse. We used a whole report experiment combined with analysis based on a Theory of Visual Attention (TVA; Bundesen, 1990) for simultaneous estimation of these two capacity parameters in 22 patients with right side stroke. Lesions were examined by MRI. Visual processing speed was impaired in the contralesional hemifield for most patients, but typically preserved in the ipsilesional field, even after large cortical lesions. The storage capacity of VSTM was also normal for most patients. Lesions mainly affected anterior regions of the right hemisphere, indicating that these areas are not critical for VSTM capacity or ipsilesional processing speed. However deficits in VSTM capacity were consistently found in patients with severe leukoaraiosis or large strokes extending deep into the posterior white matter. Bilateral deficits in processing speed occurred less frequently, and were related to leukoaraiosis or damage in the right temporo-parietal junction. The results are compatible with recent functional imaging studies, but elaborate these investigations by pointing to the critical importance of white matter.

1. Introduction

The amount of information that can be reported from a single fixation seems to be limited by two main factors (Shibuya & Bundesen, 1988). The first is the rate of visual information uptake (items per second) from the display. The second is the storage capacity of visual short-term memory (VSTM), which sets an upper limit for the number of objects that can be perceived simultaneously. Of the two functions, VSTM has received the largest research interest. In early studies Sperling (1960, 1967) showed that normal observers can report a maximum of about four unrelated items from a brief visual display. This limitation presumably reflects the maximum storage capacity of VSTM, a basic result that has been confirmed several times since (Shibuya & Bundesen, 1988; Vogel, Woodman, & Luck, 2001). Recently there has been a growing interest in various cognitive properties of the VSTM system (Alvarez & Cavanagh, 2004; Klaver, Smid, & Heinze, 1999; Lee & Chun, 2001; Luck & Vogel, 1997), and the first functional imaging studies of VSTM capacity have appeared (Todd & Marois, 2004; Vogel & Machizawa, 2004). These studies point to the posterior parietal cortex as critical for short-term retainment of visual stimuli.

VSTM capacity is often estimated using change detection experiments (e.g., Luck & Vogel, 1997). However in his classical studies Sperling used a whole report paradigm, in which a set of unrelated items (letters) were displayed at variable exposure durations. Besides more reliable estimation of VSTM capacity, this design has the advantage that it allows for simultaneous estimation of visual processing speed (Shibuya & Bundesen, 1988). Visual processing speed represents the total amount of information processed per second by the visual system. This functional parameter has

been less investigated, perhaps because its effect on performance is difficult to separate from the VSTM limitation. However Bundesen's (1990) Theory of Visual Attention (TVA; see below) provides a method to disentangle these two capacity limitations.

A number of recent studies have used the TVA model to investigate visual attention capacity after brain damage. Duncan et al. (1999) found that both VSTM capacity and visual processing speed were reduced bilaterally in a group of nine patients with neglect after right hemisphere damage. Duncan et al. (2003) showed that visual processing speed was severely reduced (but VSTM capacity only moderately) in two patients with simultanagnosia, and Habekost and Bundesen (2003) found bilateral reductions of VSTM capacity in a patient with a right frontal-subcortical lesion. Whereas these studies demonstrated the efficiency of TVA analysis for measuring visual attention capacity, the number of patients was not sufficient for a general mapping of critical regions. A very recent TVA study by Peers et al. (in press) is more relevant in this context. Peers et al. examined 25 patients with focal lesions in either the parietal or frontal cortex, and found that deficits in visual processing speed or VSTM capacity occurred selectively after parietal lesions. For both functions there was a significant correlation in the parietal group between reduced capacity and relatively inferior lesions, in the region of the temporo-parietal junction. However the exact critical areas were unclear, and Peers et al. suggested that damage in the underlying white matter could also be important. The present study offers a large new data set on this issue. We used TVA theory to derive estimates of VSTM capacity and visual processing speed in twenty-two patients with right side brain damage, and compared these data to individual differences in lesion anatomy. Besides clarifying the importance of cortical structures for visual attention capacity, we aimed to test the hypothesis that

damage to the underlying white matter is also critical. Influential theories claim that short-term memory (Fuster, 1997; Goldman-Rakic, 1995) and conscious recognition (Crick & Koch, 1995; Duncan, 1996) depend on integrated activity across widespread cortical areas. If this is also the case for the related functions of VSTM and visual processing speed, long-range connections should be critical for both functions. The results supported this hypothesis.

1.1. Theory of visual attention (TVA)

The TVA theory forms a basic analytic frame for our study. The theory was presented by Bundesen (1990) and accounts for findings from a wide range of experimental paradigms such as single-stimulus recognition, whole report, partial report, detection, and visual search (for a recent review of TVA and the attention literature, see Bundesen & Habekost, 2005). The model has also been integrated with theories of memory, categorization, and executive function (Logan, 2002; Logan & Gordon, 2001). Whereas the original TVA model was framed at a cognitive description level, its principles have been shown to have a strong analogy at the single cell level (Bundesen, Habekost, & Kyllingsbæk, in press). As mentioned above, TVA analysis is also being increasingly used for studies of attention deficits after brain damage.

TVA describes visual recognition and selection as a parallel processing race, where objects in the visual field compete for encoding into a limited number of VSTM slots. Encoding into VSTM implies conscious recognition. The total amount of processing capacity is limited, and distributed across objects according to their relative attentional weights. The exact properties of the processing race depend on individually variable parameter values, which are specified in a set of equations. We refer to earlier

expositions (Bundesen, 1990; Duncan et al., 1999) for mathematical details. In relation to visual attention capacity two TVA parameters are important: (a) the *visual processing speed*, *C*: the total number of visual objects processed per second, and (b) the *storage capacity of visual short-term memory* (VSTM), *K*: the maximum number of objects that can be reported from a brief visual display. Given performance data from whole report experiments, TVA analysis can estimate these parameters (as well as supplementary parameters t_0 and μ, see section 3.1). *C* can be reduced selectively in the contralesional side after brain damage, whereas *K* probably reflects a general limitation (Duncan et al., 1999). Accordingly, a single *K* value was estimated across the visual field, whereas *C* was allowed to vary between sides. In this study we focus on general reductions in visual attention capacity, which should involve *C* values in both sides (i.e., also the ipsilesional field).

2. Methods

2.1. Participants

Medical records of all patients admitted to a brain injury rehabilitation center (during a period of three years) and two university hospital stroke units (during a period of approximately two years) in Copenhagen were screened for radiological evidence (CT or MR) of stroke in the right side of the brain. To be selected for participation, a patient should also be at least six months post-injury and satisfy the following inclusion criteria: (a) normal visual acuity (Snellen score $\leq$ 9/6) and no field cuts, (b) no dementia (MMSE score $\geq$ 24), (c) no aphasia, (d) no history of major psychiatric or other

neurologic disease, (e) no substance abuse, (f) age $\leq$ 70 years,[1] (g) no oculomotor abnormalities, (h) auditory span of at least four elements, and (i) no additional damage in the left side of the brain.[2] All patients who satisfied these criteria were invited to participate in the study; twenty-one patients agreed. In a second round of selection, one year of medical records from a stroke unit in Copenhagen were screened for patients with focal lesions in the thalamus, which lead to the participation of one additional patient. All patients gave informed written consent according to the Helsinki Declaration, and approval was given by ethical committees in Copenhagen City and Copenhagen County (project no.: KF 01-116/02). The mean age of the patients was 55.1 years (*SD* = 9.5 years), and the group consisted of 10 men and 12 women. Post-injury time ranged from 6 to 41 months (mean: 20 months). All patients except two were right handed according to the Edinburgh Handedness Inventory. Twelve neurologically healthy participants formed an age-matched control group (5 men and 7 women; mean age: 56.6 years, *SD* = 5.4 years).[3] The controls were recruited by local advertisements and paid for their participation, and also gave informed written consent. In addition to the psychophysical testing, participants were given a screening battery of neuropsychological tests: Snellen chart, MMSE (patients only), Weintraub and Mesulam's (1985) cancellation test (letters and figures, unstructured versions), Wilson, Cockburn, and Halligan's (1987) line bisection test, Rey Figure Copying, auditory span, Edinburgh Handedness Inventory, and a test for extinction (detection of finger movements unilaterally vs. bilaterally). Visual fields were assessed by confrontation

[1] In the initial phase of the project two patients aged above 70 years were examined, because at this point it was unclear whether enough patients could be recruited. Independent of focal lesions, general processing capacity may be affected by non-specific factors related to aging, and the data from these two patients were not included in the analysis.

[2] After the psychophysical examination had been conducted, the MR scan of three patients revealed strokes in the left side of the brain. The data from these patients were excluded from the analysis.

[3] The data from two control participants were excluded because of a consistent failure to comply with the instructions, and use of strong analgesic medication during testing, respectively.

(patients only). General deficits in visual attention capacity have been linked to the visual neglect syndrome (Husain & Rorden, 2003), but clinical testing showed that neglect was generally weak or absent in our patients.

2.2. Experimental procedure

The experiments were set up using E-prime software (version 1.1) and run on an IBM-compatible computer. Participants were seated with their eyes approximately 100 cm from the screen in a semi-darkened room. Visual stimuli were shown on a computer monitor capable of 200 screen refreshes / second (5 ms resolution). Five letters were selected randomly and without replacement from the set {ABEFHJKLMNPRSTWXYZ} and flashed for 5 - 200 ms on the screen, followed by either a blank screen or a 500 ms bright pattern mask (see Figure 1). Each letter was shown in one of ten possible positions at the circumference of an imaginary circle centred at fixation. The radius of the circle was approximately 5 visual degrees (viewing distance was not precisely controlled). The letters were either green or purple (with equal luminance: 36 cd/m^2); the colour was selected randomly for each letter.

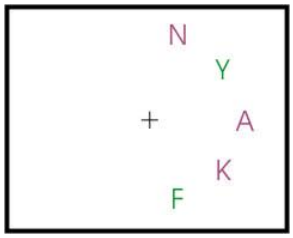

Figure 1. *Whole report. Five letters were presented in a semi-circle either to the left or right of fixation.*

Participants were instructed to report as many letters as possible, but refrain from guessing. Report was unspeeded. The exposure duration was varied systematically, with

six individually set exposure durations (based on performance in the practice trials). Four masked exposures were used, spanning an interval from the participant's approximate threshold (20 - 40 ms) to 200 ms. To prolong the effective exposure duration, two unmasked displays (usually 100 and 200 ms) were also used. There were 25 repetitions for each of these 2 * (4 + 2) = 12 conditions, randomly intermixed within each testing block. The error rate was recorded throughout, and the percentage correct score was given as feedback to the participant after each testing block. A score of 80 - 90% was encouraged to prevent too liberal or too conservative reporting. Percentage correct was on average 84.3 % (*SD* = 5.9 %) and 87.1 % (*SD* = 5.2 %) in the control and patient groups, respectively. The total testing included 300 trials, organized in blocks of 60 trials, and all testing was completed within one or two sessions of maximally one hour's length, including breaks. In addition, participants were given 20 - 30 unscored warm-up trials at the beginning of each session.

To ensure central fixation before stimulus exposure in each trial, participants were instructed to look at a centrally placed cross and, after having signalled ready, to name a random digit that appeared for 300 ms at this position. Immediately afterwards the stimulus display was initiated by the experimenter. The instruction to fixate centrally was emphasized throughout testing. As an additional control the eye movements of all participants were recorded by a video camera, and the signal was mixed with a simultaneous camera recording of the computer display. The experimenter monitored the subject's eye movements continuously on a TV screen during testing, and the mixed image was recorded on VHS tape. The VHS tapes were subsequently inspected for unwanted eye movements (i.e., away from the central cross before stimulus exposure) using 32 random samples for each participant. If an unwanted eye

movement was detected in any of these 32 trials, the whole VHS tape was inspected and all invalid trials removed from the data set. This was done for one patient, who had 29 trials removed from his data set. The patients in the project were also examined using two other experiments (partial and colour report), which targeted other psychophysical parameters than the general capacity of visual attention. These investigations are reported in a parallel article (Habekost & Rostrup, submitted), which focuses on intra-individual side differences in performance.

2.3. Data analysis

The best-fitting TVA parameter values to the observed data of each participant were estimated by a maximum likelihood fitting algorithm. The model fitting procedure used to analyze the results was basically the same as that employed in previous TVA studies, and we refer to Duncan et al. (1999) for mathematical details. Customized software for TVA analysis developed by S. Kyllingsbæk (www.psy.ku.dk/cvc/tva) was used, which also allowed for bootstrap analysis of the fits (Habekost & Bundesen, 2003; also see Efron, 1979; Efron & Tibshirani, 1993). The following parameters were estimated: K, C_{left}, C_{right}, $t_{0\text{left}}$, $t_{0\text{right}}$, and μ. In order to make the model fitting more robust, t_0 values were constrained to be 15 ms at minimum. K values were constrained not to be higher than the best score obtained by the participant. All observed data was included in the analysis (no exclusion of outlier trials). The reliability of each parameter estimate was evaluated by 1000 bootstrap repetitions. Each bootstrap sample was constrained to include at least one trial with the subject's maximum score.

2.4. Lesion analysis

The lesions of all patients except two were identified by MRI. 16 patients were examined in a 3T scanner (Siemens Trio), and 4 patients were examined in a 1.5T scanner (Siemens Vision). For a high precision description of the structural anatomy, a 3D volumetric MPRAGE sequence (1 mm^3 resolution; 3T: TR/TE/TI: 6.0/3.93/800 ms, flip angle: 8 deg; 1.5T: TR/TE/TI: 13.5/7 /100 ms, flip angle: 15 deg) covering the whole brain was performed. To characterize the lesions in further detail, patients were also examined using a FLAIR sequence (3T: TR/TE/TI: 9000/102/2500 ms, flip angle: 150 deg; 1.5T: 9000/110/2400 ms, flip angle: 180 deg). Using the combined information from these scans, the lesions were drawn on each individual's MPRAGE slices by an experienced neurologist who was blind to the psychophysical data. The MPRAGE scans with traced lesions were normalized to a 1 mm isotropic T1 template using SPM2 (www.fil.ion.ucl.ac.uk/spm/software/spm2). Before normalization the lesion area was masked out from the intact part of the brain to prevent distortions (Brett, Leff, Rorden, & Ashburner, 2001). The volume of the (normalized) lesion was computed using the MRIcro program (Rorden & Brett, 2001; www.mricro.com), and subtraction analysis was also carried out using this software (Karnath, Himmelbach, & Rorden, 2002). In addition to the analysis of stroke-related brain damage, white matter hyperintensities (leukoaraiosis) visible on the FLAIR images were traced by the first author. White matter hyperintensities are typically symmetrical in the two hemispheres, and each patient's total volume was estimated by doubling the count from the left hemisphere, which was not affected by stroke. CT scans from the acute phase of two patients were collected from hospital records. The CT scans were not analyzed quantitatively, but the lesions were traced and a verbal description was given by the

examining neurologist. Each patient was assigned to one of three subgroups: (a) large cortico-subcortical strokes with mild or no leukoaraiosis (n = 13), (b) focal strokes with mild or no leukoaraiosis (n = 6), and (c) strokes with severe leukoaraiosis (n = 3). See Table 1 for lesion characteristics.

Table 1: Lesion characteristics

Subject	Aetiology	Stroke	Leukoaraiosis
Leukoaraiosis group			
L1	Infarct	31.5	15.4
L2	Haemo	13.6	11.4
L3	Haemo	2.0	12.9
Large lesion group			
LL1	Haemo	47	0.0
LL2	Infarct	63.9	0.0
LL3	Haemo	95.9	0.3
LL4	Haemo	167.7	0.3
LL5	Infarct	137.5	0.4
LL6	Infarct	189.9	0.7
LL7	Infarct	142.7	0.0
LL8	Infarct	-	-
LL9	Infarct	153.3	0.0
LL10	Infarct	35.1	0.0
LL11	Infarct	58.8	0.3
LL12	Infarct	232.9	0.9
LL13	Infarct	214	1.6
Focal lesion group			
F1	Infarct	0.6	0.0
F2	Infarct	0.6	1.6
F3	Haemo	2.5	0.0
F4	Infarct	-	-
F5	Infarct	0.5	0.3
F6	Infarct	0.1	0.0

Aetiology: haemorrhage or infarct; Stroke: lesion volume of stroke-related brain damage (in cm^3; missing for CT scans). Leukoaraiosis: estimated volume of leukoaraiosis (in cm^3; missing for CT scans).

3. Results

In this section, we present test results (TVA estimates) and relate this set of findings to lesion anatomy. The focus is on absolute levels of performance. For a discussion of intra-individual side differences in the whole report experiment (and partial and colour report experiments) see Habekost and Rostrup (submitted). The reliability of each TVA estimate was quantified by bootstrap analysis (Efron, 1979). Given a set of observations (e.g., the 300 trials in whole report) bootstrap analysis computes an estimate of the (standard) measurement error related to each test result. The bootstrap analysis showed that measurement error was generally low: On average 10.2% for *C* and 2.7% for *K*, consistent with previous findings that TVA estimation of these parameters is highly reliable (Habekost & Bundesen, 2003).

3.1. Whole report experiment

In whole report tasks the subject must report as many items as possible from a briefly exposed array of simple unrelated stimuli (e.g., letters). The score (number of correctly reported items) is measured as a function of exposure duration, and follows a characteristic pattern (Bundesen & Harms, 1999; Duncan et al., 1999; Habekost & Bundesen, 2003; Shibuya & Bundesen, 1988; see also Figure 2). Below a minimal exposure duration, t_0, no items are reported. With postmasked alphabetic stimuli the perception threshold t_0 is typically 15 - 20 ms in young healthy subjects (Shibuya & Bundesen, 1988; Bundesen & Harms, 1999). Perception thresholds are of secondary interest in the context of visual attention capacity, and will not receive special attention (they were normal for most patients). Above the minimal effective exposure duration the curve rises sharply, but gradually flattens out over the course of a few hundred

milliseconds. Given long enough exposure time performance approaches an asymptotic value, usually interpreted as the maximum storage capacity of VSTM: *K*. The VSTM limit is typically estimated at 3 - 4 objects in healthy subjects (Sperling, 1967). Data fits of this parameter are improved by using non-integer values. For example, a *K* value of 3.3 represents a probability mixture of VSTM capacity at 3 and 4 elements, occurring with 70% and 30% probability, respectively. The *C* parameter is a measure of the total processing speed during visual recognition, and corresponds to the slope of the whole report function at $t = t_0$. *C* is highly dependent on the sensory properties and general discriminability of the stimuli. With high-contrast alphabetic stimuli, which are simple and highly familiar visual forms, *C* typically varies between 15 – 50 elements / s in healthy subjects. If stimuli are presented unmasked, an afterimage of the stimulus is briefly sustained and the exposure duration effectively prolonged. The additional exposure duration is quantified by the μ parameter, which is necessary for model fitting but will not be considered in further detail.

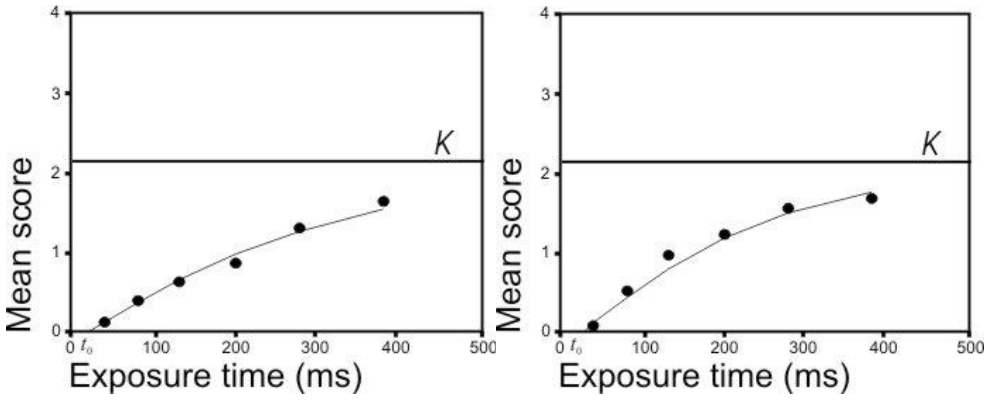

Figure 2. *Whole report performance of a patient (LL12) with deficits in both visual processing speed and VSTM capacity. Each panel shows the mean number of correctly reported letters as a function of exposure duration, separately for the left (left panel) and right (right panel) visual fields. Solid curves represent maximum likelihood fits to the observations. The estimate of VSTM capacity, K, is marked by a horizontal line, and t_0 denotes the visual threshold. The slope at the curve at $t = t_0$ corresponds to the visual encoding rate, C.*

For a summary of the whole report estimates, see Table 2. The average *K* value in the control group was 3.32 (*SD* = 0.5), consistent with previous findings in healthy subjects (Habekost & Bundesen, 2003; Vogel, Woodman, & Luck, 2001). In the large lesion group, the mean *K* value was 2.99 (*SD* = 0.8). The difference to the control mean was not significant. However there was a clear split in the group, with 10 patients having normal *K* values (i.e., $K \geq 3.0$), but three patients with *K* values in the range of 1.15 - 2.12, between two and four *SD*s below the control mean. In the leukoaraiosis group, the average *K* value was 2.15 (*SD* = 0.1), which was significantly different from the control mean ($p < 0.01$, Mann-Whitney). All three patients in this group had very low *K* values. Among patients with focal lesions, one patient with parietal damage and one basal ganglia patient had marked reductions of VSTM capacity, whereas the other four patients had normal *K* values. Thus *K* values fell into two distinct groups. Out of the 22 patients, 8 had clear reductions in VSTM capacity: 3 with (very) large lesions, 3 with leukoaraiosis, and 2 with focal lesions. Besides these deficits, it is remarkable that most patients with large lesions had preserved VSTM capacity.

Table 2: Whole Report Estimates

C_{left} / s^{-1}	C_{right} / s^{-1}	K
Control group (n=12)		
18.1 (5.0)	20.8 (5.2)	3.32 (0.5)
Leukoaraiosis group (n=3)		
8.6* (1.7)	12.3* (5.3)	2.15* (0.1)
Large lesion group (n=13)		
12.3* (5.4)	19.5 (7.4)	2.99 (0.8)
Focal lesion group (n=6)		
14.7 (3.9)	18.8 (7.5)	2.90 (1.0)

**: significant ($p < 0.05$, Mann-Whitney) deviation from the control group mean. The standard deviation of scores within each group is indicated in brackets.*

In the control group, the average C_{left} value was 18.1 letters / s (SD = 5.0 s^{-1}) and the mean C_{right} value was 20.8 s^{-1} (SD = 5.2 s^{-1}). In the large lesion group, the average C_{left} value of 12.3 s^{-1} (SD = 5.4 s^{-1}) was much lower than the control group's ($p < 0.05$, Mann-Whitney), but the mean C_{right} value was normal: 19.5 s^{-1} (SD = 7.4 s^{-1}). Thus visual processing speed was reduced selectively in the contralesional field after most large lesions. Only two patients in this group had a markedly reduced (about 2 SD below the control mean) C value in both visual fields. In the leukoaraiosis group the mean C_{left} and C_{right} values were 8.6 s^{-1} (SD = 1.7 s^{-1}) and 12.3 s^{-1} (SD = 5.3 s^{-1}), respectively. The mean C values were significantly different from the control group

mean in both sides (both: $p < 0.05$, Mann-Whitney). Finally, patients with focal lesions had average C_{left} and C_{right} values at 14.7 s^{-1} (*SD* = 3.9 s^{-1}) and 18.8 s^{-1} (*SD* = 7.5 s^{-1}), respectively. The difference to the control mean did not reach significance in either visual field, but one patient with parietal damage was about 2 *SD* below the control mean in both sides. To sum up, visual processing speed was impaired in the left side for most patients. As discussed in a parallel article (Habekost & Rostrup, submitted), the contralesional reduction in visual processing speed was associated with lesions in the right putamen area, which were highly frequent in the patient group. In the present context we focus on general reductions in visual attention capacity, which implies that the ipsilesional hemifield is also affected. Bilateral deficits in visual processing speed occurred much less frequently than selective contralesional reductions, but were found after leukoaraiosis and in two patients with large lesions as well as a single patient with focal damage.

3.2. Lesion anatomy and psychophysical performance

In the large lesion group ten out of thirteen patients had normal *K* values in spite of extensive damage to the right side of the brain. See Figure 3 for a density plot of the normalized lesions of these patients[4]. The lesions centred on the putamen, where all patients but one was affected, and typically also involved large segments of the insula and inferior frontal lobe. This is strong evidence that these areas are not critical for VSTM capacity.

[4] The lesion of one patient (LL8) in this group was not included in the overlap analysis, since only a CT scan was available. The lesion was located within the same area as the others.

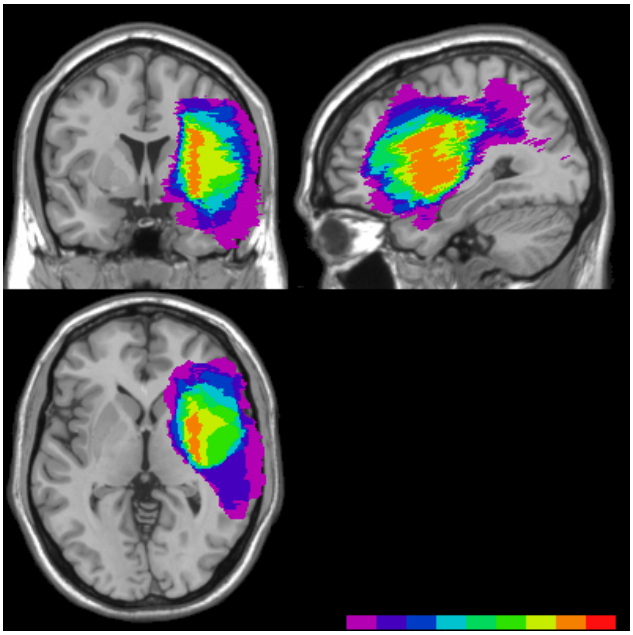

Figure 3. *Density plot of normalized lesions for nine patients with large strokes but normal VSTM capacity. The number of overlapping lesions is illustrated by different colours coding increasing frequencies from violet (n = 1) to red (n = 9).*

Three patients in the large lesion group had marked *K* reductions. These patients also had the largest lesions in the group. Accordingly, there was a significant negative correlation between *K* and lesion volume in the large lesion group as a whole: r_s = -0.70 (n = 12, $p < 0.05$). However, among patients with normal *K* values there was no significant correlation: r_s = -0.33 (n = 9, $p = 0.39$) in spite of highly variable lesion size within this group (range: 35.1 - 167.7 cm^3; *SD* = 51 cm^3). An explanation for the discrepancy is that very large lesions were systematically related to damage in particular regions, and that damage here - rather than lesion volume per se - was critical. As illustrated in Figure 3 patients with large lesions had a common damage focus (which was also shared by the three patients with reduced *K* values) in an anterior area that included the putamen and overlying frontal and insular cortex. Other cortical areas were affected to a more varying degree: The larger the lesions, the more they extended away (posteriorly, superiorly and laterally) from the putamen focus. For the three patients

with VSTM deficits and very large lesions, this implied damage in remote areas not shared by the ten patients without VSTM deficit. To describe these unique areas of damage we subtracted the normalized lesions of patients with normal *K* values from each of the three patients' lesions, and examined the overlap of the remaining lesion parts. Three main foci emerged, all located in the white matter: High in the centrum semiovale, beneath the middle temporal gyrus, and near the temporal pole (see Figure 4). Potentially, each of these areas could be critical for VSTM capacity.

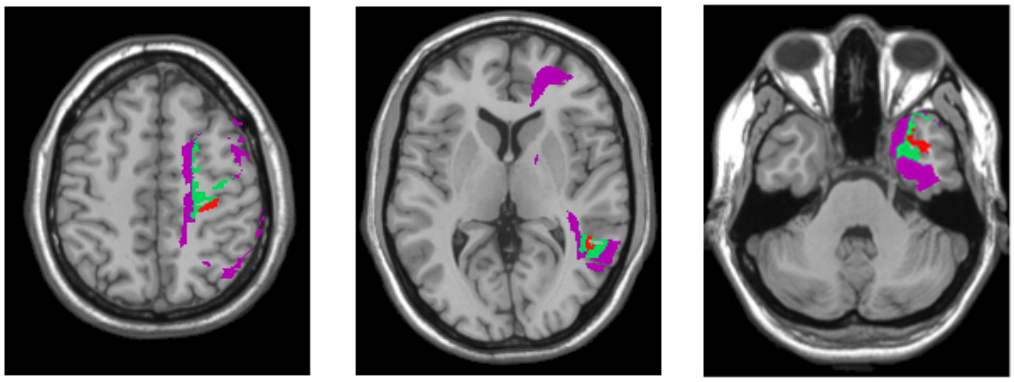

Figure 4. *Density plot of normalized areas of damage in three patients with large lesions and reductions of VSTM capacity, with the lesions of nine patients with normal VSTM capacity subtracted out. Red areas: all three lesions overlap; green: two lesions overlap; purple: single lesion.*

The most peripheral parts of these large lesions were often not completely infarcted, but rather partially damaged (e.g., de-myelinated) white matter tissue. This is for example evident in the MR scan of the patient (LL13) with the most extreme reduction of VSTM capacity (*K* = 1.15; see Figure 5).

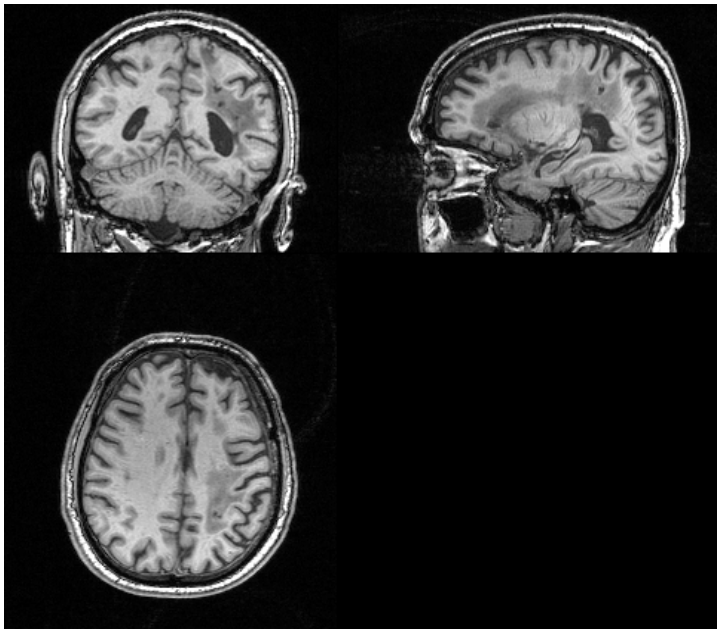

Figure 5. *MR scan of the patient (LL13) with the largest VSTM deficit. Note the widespread affection of white matter.*

In the patient group as a whole, the estimated volume of white matter hyperintensities (leukoaraiosis) had a strong negative correlation with *K*: r_s = -0.68 (n = 20, $p < 0.005$). This effect was due to three patients with severe leukoaraiosis (see Figure 6), who all had marked reductions in VSTM capacity. The leukoaraiosis was close to symmetric in the two hemispheres, and periventricular as well as centrum semiovale regions were affected. Two of the patients had small strokes in areas (thalamus, putamen) that, judging from other patients, were not critical for VSTM capacity. However the infarct of the third patient included periventricular white matter, which might have contributed to the observed deficit in *K*.

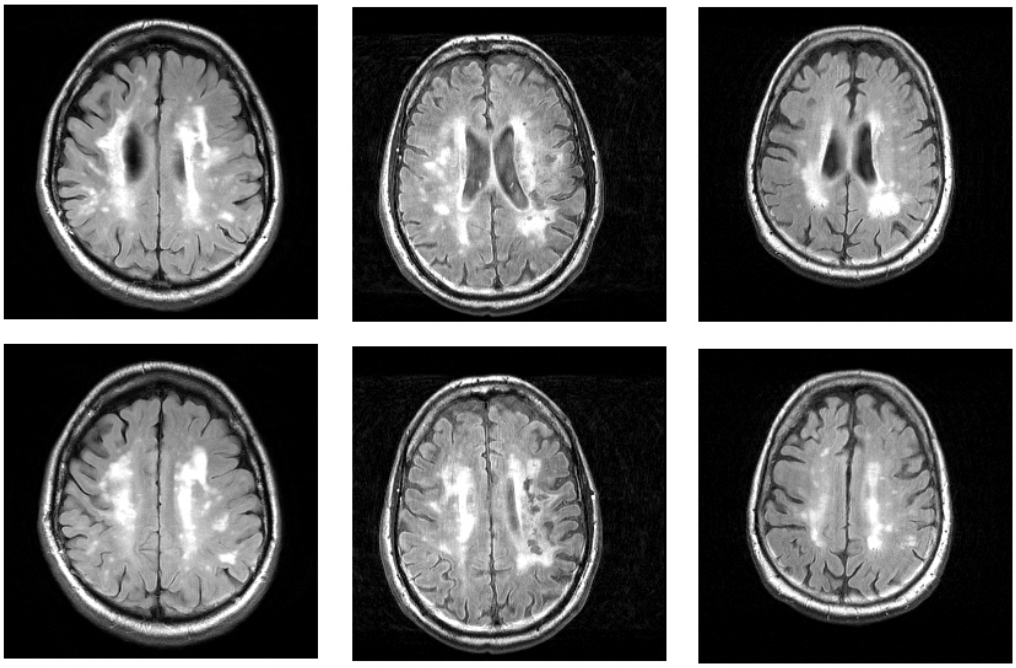

Figure 6. *FLAIR scans of three patients with severe leukoaraiois and marked reduction of VSTM capacity. Upper panels: periventricular damage. Lower panels: centrum semiovale damage.*

Two patients had marked *K* reductions after focal lesions. The first of these patients had a small lesion in the intraparietal sulcus, which fits well with a recent fMRI study of VSTM capacity (Todd & Marois, 2004). However only a CT scan was available for this patient, which is not optimal for detection of leukoaraiosis. Therefore the influence of this factor cannot be ruled out. The second patient with *K* reduction had a small lesion in the putamen and corona radiata. The reason for the poor performance of this patient is unclear, but MRI cannot reveal all effects of brain damage and subcortical lesions may sometimes, due to their connectivity, profoundly affect the function of larger, structurally intact parts of the brain (Vallar, Cappa, & Wallesch, 1992).

Visual processing speed in the contralesional side, C_{left}, was often impaired, but reductions of C_{right} occurred rarely. Eleven out of 13 patients in the large lesion group had a C_{right} value within normal variability, which shows that the anterior area

commonly damaged in this group was not critical for ipsilesional processing speed. The two patients who did have marked deficits of C_{right} shared a lesion area in the temporo-parietal junction, which was not affected in the eleven other patients (see Figure 7). The result corresponds to a previous report by Peers et al. (in press) relating TPJ and visual processing speed. Viewed as a test of this hypothesis, the finding that the two patients in the group who had a C_{right} deficit were also the ones with TPJ damage was significant at $p = 0.013$ (Fisher's exact probability test).

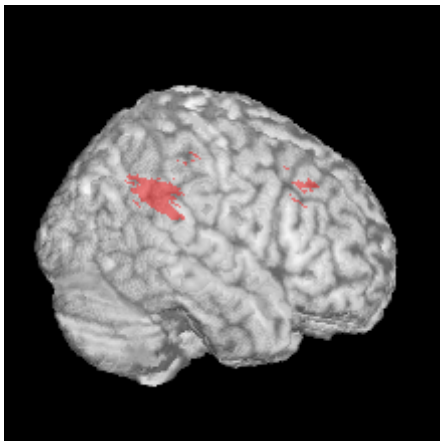

Figure 7. *Two patients with large lesions and ipsilesional reductions in visual processing speed shared an area of damage in the temporo-parietal junction that was intact in the other patients. The normalized area is shown in red (produced by subtracting out lesions belonging to patients with normal C_{right} values).*

C_{right} and lesion volume were not reliably correlated in the patient group as a whole: $r_s = -0.17$ (n = 20; ns.), but there was a significant negative correlation between C_{right} and the estimated leukoaraiosis volume: $r_s = -0.57$ (n = 20; $p < 0.01$). However the relation between deficit and leukoaraiosis was not as consistent as for VSTM capacity: Of the three patients with severe leukoaraiosis, one had a C_{right} value that was close to normal, and another was only moderately reduced (1.5 *SD* below the control mean).

4. General discussion

The information uptake from a brief visual display seems to depend on two factors: The rate of visual encoding, *C*, and the storage capacity of VSTM, *K*. Recent functional imaging studies of VSTM capacity have emphasized a cortical localization of the function, specifically the posterior parietal lobe. However functional imaging carries an inherent bias by being targeted at grey matter processes. In addition these methods only show regions that are (relatively) active during a given task, which is not equal to being functionally critical. Lesion studies provide a stronger design for finding critical regions, though localization is typically less precise. We found evidence that white matter damage is related to bilateral deficits in visual attention capacity, whereas lesions in a large, anterior part of the right hemisphere do not seem to be critical. We also found support for the hypothesis that damage in the temporo-parietal junction is related to general deficits in visual processing speed (Peers et al., in press). We integrate these findings with functional imaging studies for a more comprehensive account of the neural basis of visual attention capacity.

4.1. Non-critical areas for visual attention capacity

Ten out of thirteen patients with large right hemisphere strokes had normal VSTM capacity, and eleven patients in this group had intact visual processing speed in the right visual field. The lesions of these patients centred on structures in the basal ganglia, insula, and inferior frontal cortex (cf. Figure 3), and involvement of the posterior parietal cortex was minor or absent in most cases. VSTM capacity and ipsilesional visual processing speed was also normal in two patients with right thalamic

lesions and two patients with focal damage in the right basal ganglia. These results show that a large, anterior part of the territory of the right middle cerebral artery (as well as segments of the right thalamus) is not critical for the general capacity of visual attention, at least in terms of VSTM capacity and visual processing speed. The findings are consistent with another TVA patient study by Peers et al. (in press), who found no deficits in *C* or *K* after focal lesions in the left or right frontal cortex. The present results are perhaps more surprising because many of our patients had rather large cortico-subcortical lesions.

The results bear on theories which argue that the right hemisphere contains a representation of both visual fields (Heilman & van den Abell, 1980; Mesulam, 1981) or that it plays a special role in general alertness (Heilman, Watson, & Valenstein, 2003; Posner & Petersen, 1990). Both notions imply that right side brain damage can lead to bilateral impairments of attention. This certainly seems to be the case, especially in relation to the neglect syndrome (Husain & Rorden, 2003), but the present findings show that a substantial part of the hemisphere is not critical for two main types of general attention capacity: (ipsilesional) visual processing speed and VSTM capacity.

4.2. Cerebral connectivity and visual attention capacity

According to a standard view, short-term retainment of visual information implies that the activation of neurons representing the information is sustained in a feedback loop (Hebb, 1949; Tallon-Baudry, Bertrand, & Fischer, 2001). The feedback process is usually assumed to depend on interactions between prefrontal and posterior cortical areas (Fuster, 1997; Goldman-Rakic, 1995) and possibly also cortico-thalamic networks (Bundesen et al., in press). This way VSTM should involve information

transfer between remote brain areas and depend on efficient long-range fibres. A related view holds that conscious recognition of visual objects (reflected in the *C* parameter) requires broadly distributed activity in parietal and frontal cortex (Beck, Rees, Frith, & Lavie, 2001; Crick & Koch, 1995; Duncan, 1996; Rees et al., 2000) besides in visual areas. As with VSTM, successful integration of this complex activity should depend on fast reciprocal connections. On theoretical grounds, one should therefore expect reductions in both *K* and *C* after damage in relevant parts of the white matter, specifically the long-range posterior-anterior or cortico-thalamic connections. The data confirmed this prediction.

Two lesion patterns in our study were systematically related to reductions in VSTM capacity: Severe leukoaraiosis and very large strokes in the right side of the brain. Both types of damage should compromise cerebral connectivity. Leukoaraiosis is a descriptive radiological term for diffuse abnormalities in the white matter, seen as high intensity signals on T_2-weighted or fluid-attenuated inversion recovery (FLAIR) MR scans (Ward & Brown, 2002). The abnormalities may be caused by multiple sclerosis or metabolic disease, but usually result from subcortical arteriosclerosis. A main effect is de-myelinization of fibre tracts, presumably leading to slower signal transmission. Some degree of leukoaraiosis is a common finding in the elderly population, especially when examined by sensitive MR sequences. The clinical implications of the condition are controversial, and it has been argued that leukoaraiosis is often asymptomatic (Bonanno et al., 2000). However other studies have found associations with dementia (Inzitari et al., 1987), declines in general intelligence (Garde, Mortensen, Krabbe, Rostrup, & Larsson, 2000), and executive dysfunction (O'Sullivan et al., 2004). To our knowledge the condition has not previously been

associated with visual deficits, but the present study suggests that severe leukoaraiosis is related to reductions in VSTM capacity and, less consistently, general visual processing speed. Severe leukoaraiosis typically affects both hemispheres diffusely at periventricular and centrum semiovale levels (cf. Figure 6). The observed deficits in visual attention capacity could thus be related to several fibre systems, and converging evidence from other sources should guide the interpretation.

Three patients with very large right side strokes also had reductions of VSTM capacity. Compared to other patients with large strokes, these patients had unique damage in the right centrum semiovale and temporal white matter. Both regions contain a large number of intrahemispheric and cortico-subcortical fibres, which are potentially relevant for VSTM. The importance of centrum semiovale fibres is suggested by the fact that patients with leukoaraiosis were also strongly affected in this region. On the other hand, the more inferior damage in the temporal white matter corresponds to findings on critical areas for chronic neglect (Samuelsson, Jensen, Ekholm, Naver, & Blomstrand, 1997), a condition that is associated with bilateral attention deficits (Duncan et al., 1999; Husain & Rorden, 2003). As with the deficits after leukoaraiosis, the data do not point clearly towards particular fibre systems. Functional imaging studies of the cortical networks that are knit together by the fibres provide a broader context for interpretation (see next section).

Bilateral deficits in visual processing speed occurred infrequently in our patient group, but were related to damage in the temporo-parietal junction (TPJ) or leukoaraiosis. The importance of TPJ cortex replicates results by Peers et al. (in press), who found that deficits in the *C* parameter were related to lesions in this region. More generally, there is now considerable evidence that the right TPJ is central to stimulus

detection and recognition, particularly for salient or unexpected stimuli (Corbetta, Kincade, & Shulman, 2002; Downar, Crawley, Mikulis, & Davis, 2002). As for the relation of C_{right} to leukoaraiosis, rapid stimulus recognition should be impaired by diffuse damage to long-range fibres, similar to VSTM capacity.

4.3. The neural basis of visual attention capacity

The neural basis of visual attention capacity has been investigated by two main methods: functional imaging and studies of brain damage. Functional imaging studies have found bilateral fronto-parietal activity in visual working memory tasks (Corbetta et al., 2002; Linden et al., 2003). Given this, it may be surprising that we found no relation between right frontal damage and VSTM capacity. One explanation is that lesions in our study were located relatively inferior in the frontal lobe, whereas VSTM may be associated with more superior areas (Bundesen, Larsen, Kyllingsbæk, Paulson, & Law, 2002). Another possibility is suggested by recent imaging studies that specifically targeted the storage limitation of VSTM. These studies suggest that the posterior node of the fronto-parietal networks is the most relevant for storage capacity (Owen, 2004). In an fMRI study, Todd and Marois (2004) found that bilateral activity in the intraparietal sulcus and the intraoccipital sulcus correlated with the number of objects held in VSTM. Vogel and Machizawa (2004) reached a similar conclusion in an ERP study, in which activity at posterior parietal and lateral occipital electrode sites correlated with performance on a VSTM task. Rather than storage per se, prefrontal areas may be critical for higher-order operations such as shielding VSTM representations from interference (Miller, Erickson, & Desimone, 1996) or executive memory processes (Linden et al., 2003).

Based on the evidence from functional imaging one should expect lesions in the posterior parietal lobe, perhaps specifically the intraparietal sulcus, to cause reductions in VSTM capacity. Strong evidence on this issue remains elusive. VSTM deficits have been found in a group of neglect patients with damage involving the right parietal cortex (Duncan et al., 1999), but no systematic lesion analysis was attempted in this study. Peers et al. (in press) reported that VSTM deficits were related to lesions in the region of the TPJ, but this was not supported by the present study. Both Peers et al. and the present study examined very few patients with damage in the intraparietal sulcus, which makes it hard to assess the significance of this area. Instead, the present study pointed to the white matter underlying the posterior cortex. This is compatible with the importance of the posterior parietal cortex, though not direct support for this hypothesis.

The second capacity parameter, visual processing speed, should primarily depend on the efficiency of basic pattern recognition processes. Numerous studies have linked visual recognition to ventral occipito-temporal areas (Ungerleider & Mishkin, 1982; Milner & Goodale, 1995), which were generally intact in our patient group. In particular the left extrastriate cortex, which has been associated with letter recognition (Flowers et al., 2004; Polk et al., 2002) was not affected in any patients. However, in line with theories that multiple cortical areas are necessary for conscious recognition (Beck et al., 2001; Duncan, 1996), more dorsal regions also seem relevant for visual processing speed. Simultanagnosia, which typically occurs after bilateral parietal lesions, has been related to extreme reductions in visual processing speed (Duncan et al., 2003). Both the present study and Peers et al. (in press) found a relation between *C* reductions and damage in the TPJ region, which may be explained by a general alertness function of this area (Corbetta et al., 2000). The present study also found a

negative correlation between C_{right} and leukoaraiosis. In relation to TPJ function, the periventricular part of the leukoaraisis should be most relevant, but this hypothesis awaits more data to be tested.

5. Conclusion

The neural basis for general capacity limitations in visual attention is still a relatively unexplored issue. A main finding of the present study was that a large anterior region in the right hemisphere is not critical for VSTM capacity or ipsilesional processing speed. Instead the results pointed to the significance of white matter underlying the parietal and temporal cortex. In particular, the clinical state of leukoaraiosis seemed related to bilateral deficits in visual attention capacity. The study also confirmed a previous report relating the temporo-parietal junction to visual processing speed, but the evidence on this issue is still sparse.

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