Words don’t come easy

On the cerebral specialization for visual word recognition

Ph.D. dissertation

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FOREWORD

Together with the four 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.

I: Starrfelt, R. (2007) Selective alexia and agraphia sparing numbers: A case study. *Brain and Language,* 102: 52-63.

II: Starrfelt, R., & Gerlach, C. (2007) The Visual What For Area: Words and pictures in the left fusiform gyrus. *NeuroImage,* 35*;* 334-342.

III: Starrfelt, R., Habekost, T., & Gerlach, C. (2008) Visual processing in pure alexia: A case study. Manuscript submitted for publication.

IV: Starrfelt, R., Habekost, T., & Leff, A.P. (2008) Too little, too late: Reduced visual span and speed characterize pure alexia. Manuscript submitted for publication.

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Randi Starrfelt

"The existence of a selective impairment of reading, without concomitant impairments in other visual or language processes, implies that there is some region of the brain that is necessary for and dedicated to reading. If ... the word form hypothesis is true, this implies that localized brain functions include functions that are evolutionarily very recent, that require extensive instruction to learn, and that relatively few individuals in the history of the species have ever possessed. While not a priori impossible, this conclusion represents a surprising departure from other functions that we know to be localized (perception, motor control, language, memory). Thus, the issue of whether pure alexia represents a selective impairment for reading per se, or whether it is a manifestation of a more general impairment, has implications beyond our understading of reading impairments. It bears on the issue of how the functional architecture of the mind is mapped onto the physical architecture of the brain, and in particular on the distinction between the kinds of psychological processes that make use of localized dedicated hardware and the kinds that do not".

Martha Farah, 1990; 114-115.

"Appearance blinds, whereas words reveal."

Oscar Wilde, 1883.

CONTENTS

SUMMARY

This dissertation comprises a brief theoretical review and four empirical studies relating to the question of whether cerebral areas can be specialized for reading. This question has been studied within the broader context of cognitive neuroscience, both in patients with acquired disorders of reading, and with the use of functional imaging techniques. Extant evidence for (and against) cerebral specialization for visual word recognition is briefly reviewed and found inconclusive.

Study I is a case study of a patient with a very selective alexia and agraphia affecting reading and writing of letters and words but not numbers. This study raised questions of "where" in the cognitive system such a deficit may arise, and whether it can be attributed to a deficit in a system specialized for reading or letter knowledge. The following studies investigated these questions in the visual domain.

An important account postulates that an area in the mid-fusiform gyrus - *The visual word form area* - is specialized for reading (in literate adults). Study II is a PET study investigating activity in this area during performance of tasks with pictures and words. This study concludes that there is something special about word processing in this area, but that this may relate to the relative automaticity in the reading process, rather than reflect true cerebral specialization for reading. We suggest that the process of shape integration, which is common to both word and object processing, may explain the pattern of activations found in our and other functional imaging studies of the visual word form area.

Study III reports a patient (NN) with pure alexia. NN is not impaired in object recognition, but his deficit(s) affects processing speed and visual apprehension span for both letters and digits. Thus, his visual deficits are not specific to alphabetical material. NN is also impaired in the categorization of fragmented drawings, suggesting a subtle deficit in the process of shape integration. We suggest that this subtle deficit can explain why words seem to be reduced to their constituent parts (letters) in pure alexia.

Study IV reports four patients with mild pure alexia, and shows that they are all impaired in processing of both single letters and digits in the central visual field. Furthermore, all four patients have reduced visual apprehension span for both letters and digits, as well as subtle deficits with pictorial stimuli. This study supports the notion that pure alexia is associated with a general visual deficit that affects other stimuli than letters and words. We suggest that the reduced recognition efficiency in the central part of the visual field observed in our patients is the most important factor contributing to their reading problems.

In sum, the empirical studies do not support the notion of selectivity for word or letter processing in the visual domain. However, the findings do suggest that reading may be disproportionately affected by damage to more general purpose visual recognition processes.

DANSK RESUMÉ

Denne afhandling indeholder en kort teoretisk oversigt og fire empiriske studier, der omhandler hvorvidt områder i hjernen kan være specialiserede for læsning. Dette spørgsmål har været undersøgt indenfor den kognitive neurovidenskab, både hos patienter med erhvervede læseforstyrrelser, og ved brug af funktionel billeddannelse. Eksisterende evidens for (og imod) hjerneområders specialisering for læsning gennemgås kort, og findes inkonklusiv.

Studie I er en kasuistik af en patient med en meget selektiv aleksi og agrafi for bogstaver og ord, men ikke tal. Dette studie rejste spørgsmål om "hvor" i det kognitive system sådan en forstyrrelse kan opstå, og om den kunne henføres til skade i et system specialiseret for læsning eller viden om bogstaver. De følgende studier undersøgte disse spørgsmål i det visuelle domæne.

En vigtig teori hævder at et område i den venstre fusiforme gyrus - *Det visuelle ordform område* - er specialiseret for læsning. Studie II er et PET-studie, som undersøgte aktivitet i dette område under udførelse af opgaver med billeder og ord. Dette studie konkluderer, at der er noget specielt med processering af ord i dette område, men at dette kan hænge sammen med hvor automatisk læseprocessen er snarere end egentlig hjernemæssig specialisering for læsning. Det foreslås, at form-integration, en process der er fælles for ord og objekter, kan forklare det mønster af aktivering, der findes i dette og andre billeddannelses-studier af det visuelle ordform område.

Studie III rapporterer en patient med ren aleksi. NN genkender objekter normalt, men hans forstyrrelse(r) påvirker processeringshastighed og visuel spændvidde for både bogstaver og tal. Altså er hans forstyrrelse ikke specifik for alfabetisk materiale. Ved kategorisering af fragmenteret materiale har NN også vanskeligheder, hvilket tyder på en subtil forstyrrelse i form-integration. Det foreslås, at denne subtile forstyrrelse kan forklare hvorfor ord ser ud til at være reduceret til deres bestanddele (bogstaver) i ren aleksi.

Studie IV rapporterer fire patienter med ren aleksi og viser, at de alle har forstyrrelser i genkendelse af såvel bogstaver som tal i det centrale synsfelt. Endvidere har alle fire patienter nedsat visuel spændvidde for bogstaver og tal, samt subtile vanskeligheder med billedmateriale. Dette studie støtter tesen om, at ren aleksi hænger sammen med en generel visuel forstyrrelse som påvirker andre stimuli end bogstaver og ord. Det foreslås at den reducerede evne til at genkende former centralt i synsfeltet, som observeres hos alle fire patienter, er den vigtigste årsag til deres læsevanskeligheder.

De empiriske studier støtter ikke tesen om selektivitet for processering af bogstaver og ord i det visuelle domæne. Dog tyder fundene på, at læsning bliver uforholdsmæssigt påvirket af forstyrrelser i mere generelle visuelle genkendelsesprocesser.

1. Introduction

Reading is an important skill in modern society, and being unable to read or being a poor reader is a major handicap. This is why educational systems - and the young students in them - spend a great deal of time and effort on learning to read fluently. Observing children learning to read can give a hint about what a complex and challenging process reading really is, and the years it takes to learn this skill further underlines the complexity of what is to be learned. Yet this is easily forgotten by proficient adult readers, because when reading is successfully learned it is something we do with great ease. We even do it in quite an automatic way: Whenever we look at a word, we read it - or so it seems. Intriguing evidence for this relative automaticity is found in the Stroop effect (Stroop, 1935), where the time taken to name the colour of the ink with which a word is written is greatly influenced by whether the word represents the same or a different colour. Perhaps it is not so surprising that we process written words so effortlessly once we have practised reading for some years, as we have by then read so many of them. Indeed most literate adults are experts in reading, experts in the visual decoding of written words and translation of them to sound or meaning. If words are treated as a category of visual objects, then most of us will have seen more exemplars of this particular category than any other. Even the botanist probably sees more words than flowers and plants, the geologist more words than stone formations, the neurologist more words than brains, although perhaps some mathematicians see more numbers and equations than written words. Even reading a short newspaper article will present you with a few hundred words, and just reading the street- and shop-signs you pass during an ordinary day may perhaps amount to the same number. Reading for half an hour a day during a year, involves processing of at least 2 million words, constituted by about 10 million letters[1]. So perhaps it is no wonder we are experts in reading, and we perform the task so easily.

But for some people, the written world is experienced quite differently, as they have a reading disorder that prevents them from processing letters and words without effort. There are two major categories of reading disorders: The *developmental dyslexias*, that disrupts the process of learning to read during childhood, and the *alexias* or *acquired dyslexias* that results from damage to the brain in people who were able to read normally before their injury. In both disorders symptoms vary both in severity and in kind. Having a reading disorder is incapacitating in many ways, and it is important to gain insight into how reading is accomplished in normal readers, how and why this skill fails to develop with instruction in some individuals, and how it can be affected by brain

[1] Conservative estimate based on Pelli, Burns, Farell & Moore-Page, 2006, p 4648.

injury. A major motivation for studying both normal and pathological reading has been to understand how the complex process of reading works on a cognitive and a cerebral level, and one important goal of this enterprise is to develop intervention strategies to ameliorate the symptoms of these disorders.

Within neuropsychology and neuroscience one has been concerned with the general question; can brain areas be dedicated to one process or even to processing one kind of material? This has been discussed since the birth of modern neurology, when Broca suggested a specialized area for the production of spoken language. Long before that, Gall and the phrenologists had taken the idea of specialized cortical areas to an almost ridiculous extreme, suggesting for instance areas dedicated to *maternal love* or *hope*. However, Gall also suggested areas of specialization for processes or content that modern neuroscience still debates, such as place memory (modern: *Parahippocampal place area)* and even memory for words, which could translate to a *Word form system* or *area*; the topic of this thesis.

The existence of specialized higher order perceptual areas has been intensely debated in modern brain science (e.g., Kanwisher & Yovel, 2006). One part of this debate has been about the existence of the so called *Visual word form area*, first defined as the "visual area of the left ventral temporal lobe which is activated by letter strings more than by other types of stimuli" (Cohen et al., 2000, p. 303). At a more general level the discussion of specialization for written word recognition revolves around the question of whether specialized perceptual brain areas can develop through learning (Polk & Farah, 1998; Cohen & Dehaene, 2004; Price & Devlin, 2003). As opposed to recognition of faces, which is developed automatically very early in infancy, as well as the recognition of common objects, the recognition of letters and written words is learned late in childhood, and then only through instruction over a period of years. Thus, if reading can be shown to rely on specialized cerebral areas, this would be evidence for the development of such areas through learning and therefore this question has received quite a lot of attention. The study of pure alexia, an acquired disorder of reading that leaves the ability to write intact, has been important in the literature concerning cerebral specialization for reading. This disorder can be caused by a relatively circumscribed cerebral lesion and seems to selectively affect the reading process, while leaving other language functions and perhaps also other visuoperceptual functions intact. As reading is not only thoroughly learned in most literate societies, but also extensively practised, it seems clear that this must affect the brain in some ways. The question is: Can learning perceptual or motor language skills create areas in the brain *selectively* dedicated to these skills, or do reading and

writing rely upon brain structures and cognitive processes that are also involved in visual object perception, spoken language, semantics, and motor functions? While cerebral specialization could potentially refer to specialization for a given process like extracting visual features, the visual word form area is claimed to be specialized for and selectively dedicated to processing one kind of material, namely letters and words.

The theme of this dissertation is cognitive and cerebral specialization for written word recognition. Through studies of brain injured patients as well as with the aid of functional brain imaging techniques, the question of whether areas of the brain are selectively engaged in reading will be investigated. For simplicity, the hypothesis of cerebral specialization for reading may be referred to as the "specialization hypothesis" in the following, and "word selectivity" refers to the idea of cerebral areas selectively dedicated to processing written words.

1.1. A methodological concern

There is a methodological problem with the studies presented as part of this dissertation, as well as other studies investigating the same issue, that deserves to be mentioned already: If word selectivity cannot be shown with the methods at hand, that does not mean that it does not or can not exist on a neuronal level. All findings of lack of selectivity will have to leave open the possibility that the method applied was not sensitive enough. Activation of an area by two kinds of stimuli in a functional imaging study does not necessarily imply that this area is equally important for the processing of both. Also, as brain lesions commonly affect more than one cerebral area (however defined), lack of selectivity of deficits does not necessarily imply that there were no specialized regions within the lesioned area. If brain injured patients show deficits of more than one process or function, which they do more often than not, this does not mean that these functions relied on the exact same brain structures before the injury. However, findings of selectivity can be equally problematic as one runs the risk of rejecting the null hypothesis on false grounds, again depending on the sensitivity of measures. Possibly, comparing reading to bicycle-riding may reveal activation in different cerebral structures in a very hypothetical imaging study. Also, lesions causing reading deficits may not affect cycling, while brain injury leading to the lack of the ability to cycle may not affect reading. Thus, the two processes can be claimed to form a double dissociation (Shallice, 1988), and one may conclude that cycling and reading rely on different cerebral areas. So far, the argument is valid. However, these findings are not sufficient to claim that brain areas concerned with reading are specialized for this process. Admittedly the chosen example may be a little far

fetched, but this is in no way intended as ridicule, but to point to an important methodological issue concerning the current work. Within this area of research, "evidence" both for and against word selectivity has been published, and much of the disagreement seems to relate to the kind of tasks and stimulus types that are compared, as well as to the behavioural or imaging paradigms that are utilized both with patients and with normal subjects. In cognitive neuroscience, *converging evidence* from different methods is important in trying to determine the cerebral basis of cognitive processes, as well as in investigating the cognitive processes themselves. Both functional imaging studies and patients studies have limitations as to the questions they are fit to answer, while taken together they provide a stronger tool. For our purposes, functional imaging can shed light on which brain areas are activated by (and possibly involved in) normal processing of words, and lesion studies can inform us as to which of these areas (if any) are critical for word reading. But as we are not merely interested in which areas are important for reading, but also whether they are specialized for this process, the stimuli and tasks we chose to compare reading with become very important.

The specific aim of three of the reported studies (Starrfelt & Gerlach, 2007; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008) was to put the specialization hypothesis to a stringent test by using closely related stimuli as comparisons, and sensitive tasks to measure performance in both normal subjects and patients with reading disorders. The specific choice of stimuli was to a large degree inspired by the pattern of performance of the patient reported in Study I (Starrfelt, 2007), who showed an impairment in reading and writing letters while his ability to read and write Arabic numerals, as well as his ability to recognize and draw objects, was spared. The aim is not primarily to disprove (or prove) the specialization hypothesis, which as mentioned above is very likely to be impossible, but to gain a better understanding of the visual processes contributing to recognition of written words. As the specialization hypothesis is influential, but still widely debated, this is taken as the starting point in the current investigations. In particular with regards to patients with pure alexia (defined below), the question of selectivity is not just a theoretical dispute. Depending on whether this reading disorder results from damage to a word specific system or whether it is the consequence of a more general visuo-perceptual deficit, the intervention strategies to ameliorate the disorder will differ. The question of selectivity is therefore of great clinical as well as theoretical importance. In the corresponding debate about the *Fusiform face area*, it was recently pointed out that: "In the spirit of a debate that has become overly polarized [one may] choose to emphasize relatively unimportant controversial issues at the expense of bigger, more important questions" (Gauthier & Buckack, 2007, p. 323). It is the humble

aim of this dissertation to emphasize the important controversial issues concerning cerebral specialization for reading.

2. Pure alexia and visual word recognition

2.1. Defining pure alexia.

As mentioned above, alexia denotes a reading disorder acquired as a consequence of injury to the brain in previously literate subjects. Some prefer the term acquired dyslexia, but as the term dyslexia more commonly refers to a developmental disorder of reading, the term alexia is used here. Dyslexia will thus denote a developmental reading disorder throughout this dissertation, unless otherwise specified.

Pure alexia is an acquired disorder of reading, that leaves other cognitive and language functions, including writing, unaffected. It is often accompanied by a visual field defect, affecting either the entire right hemifield, or parts thereof. Whether pure alexia can exist in the absence of other visuo-perceptual deficits is a matter of debate, and is the topic of this dissertation. The cerebral lesion causing pure alexia is located in the posterior parts of the dominant hemisphere (Damasio & Damasio, 1983; Binder & Mohr, 1992), commonly including the occipital lobe. In particular, lesions affecting the left fusiform gyrus have been suggested to be of particular importance in this syndrome (Leff, Spitsyna, Plant & Wise, 2006). The suggested anatomical basis of pure alexia will be discussed in greater detail below, as this relates directly to the theme of this dissertation. A characteristic feature of pure alexia is that these patients show a word length effect in reading, that is, there is a linear relationship between the number of letters in a word, and the time taken to read it. This has been taken to reflect *letter-by-letter* reading (LBL-reading), meaning that patients are thought to identify letters in words in a serial manner. Some patients actually spell out the words they are attempting to read either explicitly or under their breath, but more often letter-by-letter reading is inferred from linear regression analyses of reaction times. The slope of the regression line then indicates the word length effect, which is given in milliseconds (or even seconds) per letter. The severity of the disorder varies widely: Some patients have only mildly elevated reaction times in reading, and show a modest word length effect (in the range of a few

hundred milliseconds), other patients take seconds to read even short words, and their word length effect can also be several seconds per letter.[2]

Although the terms *pure alexia* and *letter-by-letter reading* are commonly used interchangeably, they do not necessarily refer to the same entity. Pure alexia is defined by the presence of a reading disorder in the absence of writing deficits (agraphia) and impairments in language production or comprehension (aphasia). Indeed, in classical neurological terminology, pure alexia is referred to as *alexia without agraphia.* LBL-reading is inferred on the basis of word length effects in single word reading, effects commonly found in pure alexic patients. However, word length effects can arise due to different functional deficits (Price & Humphreys, 1992; Cumming, Patterson, Verfaille & Graham, 2006), and a letter-by-letter strategy may also be employed by patients with alexia *with* agraphia (e.g., Warrington & Shallice, 1980; Bowers, Bub & Arguin, 1996; Rapp & Caramazza, 1991) and patients with major visuoperceptual deficits (Fiset, Arguin, Bub, Humphreys & Riddoch, 2005). In the following, *pure alexia* will denote *alexia without agraphia,* while LBL-readers will refer to patients showing a word length effect in reading, regardless of aetiology, lesion site, and accompanying deficits. Thus, the discussion of LBL-reading may not at all points relate directly to the discussion of mechanisms of pure alexia. Some authors have used the term *spelling dyslexia* to refer to the same phenomenon as LBL-reading (e.g., McCarthy & Warrington, 1990; Warrington & Langdon, 2002), and these cases will be treated in the same manner as patients with LBL-reading. Note that in this particular instance, dyslexia refers to an acquired reading disorder.

In the more severe disorder of *global alexia*, patients are severely impaired in letter identification and quite incapable of word reading (Binder & Mohr, 1992). These patients may have preserved writing and language skills, and thus this disorder belongs in the category alexia without agraphia. Many patients with global alexia are referred to simply as pure alexics in the literature, but in the following a distinction based on severity will be made where evidence is available to support it. At the other end of the severity spectrum, pure alexia merges with *hemianopic alexia;* a reading deficit caused by a visual field defect. Hemianopic alexia is usually caused by hemi- or

[2] Word length effects are not necessarily directly comparable across subjects from different studies, as there are several ways to measure them. In older studies (e.g., Warrington & Shallice, 1980), these effects were often measured by timing reading of lists of words of different length by use of a stop watch. In newer studies, word reading is commonly assessed by using computer presentation of single words and a voice key to measure reaction times, although for some severely impaired patients, or patients actually spelling the words out loud, this is not possible (e.g., Leff et al., 2001).

quadrantanopia affecting the central part of the visual field (Zihl, 1995), but may be seen after more subtle field defects also (Habekost & Starrfelt, 2006). Patients with hemianopic alexia also show a word length effect in reading, although of smaller magnitude than in pure alexia, while their deficit is more pronounced in text reading (Leff et al., 2000; 2001). Although the two syndromes may form a continuum (Leff et al., 2006), this continuum remains relatively unexplored, and for the purposes of this dissertation, hemianopic alexia constitutes a disorder separate from pure alexia.

2.2. Accounts of pure alexia and visual word recognition

A classical view of pure alexia, or rather spelling dyslexia, within the cognitive neuropsychological literature, is that the disorder is the consequence of damage to a word form system, that "parses (multiply and in parallel) letter strings into ordered familiar units and characterizes these units visually" (Warrington & Shallice, 1980, p. 109). According to this view, the reading deficit arises because of damage to a system dedicated to processing written words, and is not attributable to a visual deficit (Warrington & Langdon, 2002). A more anatomically based version of this hypothesis proposes that pure alexia arises after damage to a region in the fusiform gyrus of the left cerebral hemisphere, often referred to as the visual word form area (VWFA; Cohen, et al., 2000; 2002). This area is thought to be responsible for extracting abstract letter identities invariant for parameters like size and font, and to compute abstract representations of letters presented to both hemifields (Cohen et al., 2000). Most of the evidence for the existence of the VWFA comes from functional imaging studies (e.g., McCandliss, Cohen & Dehaene, 2003), but so far there is little consensus regarding the existence of such an area, or which cognitive operations it may perform (e.g., Price & Devlin, 2003; 2004; Cohen & Dehaene, 2004). The major controversy regards whether this area is specialized for extracting abstract letter or word representations (Cohen & Dehaene, 2004), or if other visual stimuli like objects or shapes, or even non-visual stimuli, may also be processed in this region (Price & Devlin, 2003). In general, findings of selectivity for word processing in the putative VWFA from imaging studies using functional Magnetic Resonance Imaging (fMRI) or Positron Emission Tomography (PET) seem to depend on the task subjects perform in the scanner, and the stimuli employed in these tasks. The VWFA is quite consistently found activated when presentation of written words is contrasted with rest, viewing a fixation cross, or viewing simple visual patterns like checkerboards (Cohen et al., 2000; 2002). When words or letters are contrasted with more complex visual stimuli, like pictures of faces (Puce et al., 1996) or objects either in passive viewing or object matching tasks (Joseph, Gathers & Piper, 2003; Joseph, Cerullo, Farley, Steinmetz &

Mier, 2006), there is little evidence for stimulus specific activations in the VWFA. In general, there is "ample evidence that object and face recognition can also activate this area to varying degrees" (McCandliss et al., 2003; p 294), while at the same time, there are studies suggesting that it may be of particular importance in reading.

Patient studies suggest that lesions either affecting the VWFA or disconnecting it from visual input is associated with pure alexia (Cohen et al., 2003; 2004; Gaillard et al., 2006; Leff et al., 2006), although this notion has also been challenged. In a large study including 80 patients with acute stroke in the area of the posterior cerebral artery of the left hemisphere, Hillis and colleagues (Hillis et al., 2005) failed to find any significant association between damage or dysfunction in the putative VWFA and impairment in written word comprehension or lexical decision (deciding whether a letter string represents a word or not). On this basis, they suggested that visual word forms, in their words *graphemic descriptions* defined as a "font-, case-, and location-independent representation of the string of graphemes" (Hillis et al., 2005, p. 557), can be computed in both hemispheres, and thus the left lateralised VWFA is not necessary for this function. Other patient studies suggest that posterior areas in the right hemisphere are important for pure alexic reading (e.g., Cohen et al., 2003; 2004; Henry et al., 2005), but importantly, these patients do not read normally, indicating that the right hemisphere cannot fully compensate for impaired left-hemisphere processes. An important thing to keep in mind is that few if any patients have lesions restricted to the putative VWFA, and thus drawing firm conclusions about this area's contribution to visual word recognition is not possible on the basis of studies of pure alexia. The patient presented by Gaillard et al., (2006) may be an exception. Preceding surgical removal of cerebral tissue near the VWFA, this area was localized in the patient's brain by use of fMRI, and in addition the patient's reading skills were shown to be normal without a word length effect. Following surgery the patients suffered from pure alexia, and fMRI showed no activation of the VWFA in reading tasks. Recognition of other stimulus categories like faces and objects was not impaired on paper and pencil tests, and activations for these categories remained "essentially the same" after surgery.

Cohen and Dehaene (2004) have argued that the VWFA is functionally specialized for visual word recognition, a claim that is still debated. However, as part of their claim for specialization, Cohen and colleagues emphasize another feature of the VWFA; it has a *reproducible localization* across subjects (Cohen et al., 2003; Cohen & Dehaene, 2004). Regardless of the relative specialization or selectivity of processing in this area, it is interesting that a region that contributes to visual recognition of written words, a learned skill, is localized in approximately the

same area in subjects regardless of the specific language or alphabet they are able to read (Baker et al., 2007). This indicates that there are some constraints on which brain regions that come to contribute to visual word recognition, regardless of the degree of specialization of these areas.

Although less concerned with the anatomical substrate, cognitive neuropsychological studies have also addressed the question of selectivity, asking whether pure alexia really is pure in the sense that it can leave other cognitive and perceptual processes intact. As mentioned above, one cognitive theory claims that pure alexia (or spelling dyslexia) is due to damage of a word form system (Warrington & Shallice, 1980; Warrington & Langdon, 2002). Other cognitive accounts suggest that pure alexia results from more general visual impairments that affect perception and recognition of visual stimuli other than written words. One line of research has focused on deficits in perceiving other visual objects than letters and words in pure alexic patients: Behrmann and colleagues (Behrmann, Nelson & Sekuler, 1998) have shown that pure alexic patients' object recognition abilities may depend on visual complexity. They state that "pure alexia is not pure", as processing of other visual material, particularly complex pictures, is also affected. Furthermore, they have shown that patients with letter-by-letter reading show perceptual difficulties "under impoverished perceptual conditions where there is less support from organisational cues" (Sekuler & Behrmann, 1996, p. 968), and suggest that reading is one such impoverished condition. They explicitly make the claim that a general visual deficit is causing pure alexia, a claim that others have also made based on studies of visual processing in patients with pure alexia (Friedman & Alexander, 1984; Farah & Wallace, 1991).

Another hypothesis suggests that pure alexia is the result of a deficit not in object processing per se, but rather in processing many visual items in parallel (simultanagnosia) (Kinsbourne & Warrington, 1962; Farah, 1990), regardless of the category to which these items belong. Indeed, pure alexia may even be referred to as *ventral simultanagnosia* (Duncan et al., 2003; Farah, 2004). According to this view, reading depends on fast and efficient processing of many visual forms (letters) in parallel, and pure alexia reflects the breakdown of this process. Because of this deficit, patients need to process each letter in a word serially, which results in the commonly observed word length effect. Farah (2004) has recently sought to integrate this view with the findings of word selectivity in imaging studies (e.g., Cohen et al., 2000; Polk et al., 2002) by suggesting that pure alexia is the result of damage to an area specialized for rapid processing of multiple visual shapes, but which in addition has become fairly specialized for reading. This *specialization within specialization* is thought to arise because of correlation based (Hebbian)

learning. Because reading demands rapid processing of multiple visual shapes, words will be processed in the area specialized for this process. Because of environmental co-occurrence of letters in the context of letters, as well as our extensive experience with reading, letter or word specific area(s) come to be created within this larger area. This version of the simultanagnosia hypothesis thus represents a "hybrid" of a general visual and word specific account of pure alexia.

A deficit in recognizing single letters is present in most, if not all, reported cases of pure alexia (or LBL-reading; Behrmann, Plaut & Nelson, 1998). Indeed, some authors to suggest that a fundamental deficit in letter perception is the cause of pure alexia, or at least the cause of the LBL reading pattern evident in these patients (Reuter-Lorentz & Brunn, 1990; Arguin & Bub, 1993; Behrmann & Shallice, 1995;). A recent characterization of letter processing in LBL-readers suggests that letter confusability, that is, how similar a given letter is to other letters in the alphabet, is the main determinant of the word length effect observed in these patients (Fiset et al., 2005; Fiset, Arguin & McCabe, 2006). When letter confusability is controlled for, patients no longer show a word length effect in reading, although their reaction times are still prolonged compared to normal subjects. This confusability-effect is thought to arise due to an abnormally low signal-to-noise ratio when attention is distributed across a whole word, as Fiset et al. (2005) observed no correlation of performance with letter confusability when letters were presented in isolation (which does not mean that letter recognition was normal). The letter confusability account mainly aims to explain the word length effect evident in both pure alexic patients and other patients with alexia, and this account is in principle not in opposition to theories suggesting a general visual deficit as the underlying cause of pure alexia. The hypothesis even hints that the distribution of attention may be the cause of LBL-reading (a point resembling the simultanagnosia hypothesis). It has also been suggested that the letter confusability effect may arise because of decreased sensitivity to high spatial frequencies in LBL-readers (Fiset, Gosselin, Blais & Arguin, 2006).

2.3. Number reading in pure alexia

If a general visual deficit is the cause of pure alexia, one could expect this deficit to affect processing of similar symbols like digits also. As number reading is of particular interest to the investigations in this dissertation, a brief overview of earlier studies of number reading in pure alexia seems appropriate. Although it is a common belief that number reading can be unaffected in pure alexia (e.g., Geschwind, 1965; Leff et al., 2001), surprisingly few studies have examined this relationship directly. Dejerine's (1892) original pure (or global) alexic patient read multidigit

numbers digit-by-digit, the way most pure alexics read words, but he was still far better at identifying digits than letters (Bub, Arguin & Lecours, 1993). A similar pattern of performance has recently been reported in another case of global alexia (Larsen, Baynes & Swick, 2004). Henderson (1987) reported impaired reading of digits in three patients with pure alexia, and found no dissociation between the patients' performance with letters and digits in different tasks. Number reading has also been shown to be impaired in other cases of pure alexia, although commonly not to the same degree as letter and word identification (Albert, Yamadori, Gardner & Howes, 1973; Cohen & Dehaene, 1995; 2000; Miozzo & Caramazza, 1998)

There are, however, a few reports of preserved number reading in pure alexia. For instance, Luhdorf & Paulson (1977) reported a patient with severe pure alexia (or global alexia) who was incapable of naming letters but could read numbers, but few details of the assessment of number reading were given. In addition, there are reports of preserved reading of multidigit numbers in pure alexia (Leff et al., 2001) and spelling dyslexia (Warrington & Shallice, 1980), but again few details are given of the method of assessment. The evidence on record seems to suggest that number reading may be relatively preserved compared to word reading in pure alexia, and that patients rarely complain about problems in number reading. However, this question deserves to be investigated further, as it has important theoretical implications. If number reading is invariably impaired in pure alexia, this would strongly suggest that a letter or word level deficit cannot account for the disorder. This may not necessarily imply that a general visual deficit is at the core of the disorder though. As both letters and digits are learned symbols, they may recruit the same visual processing resources for identification, while these processes may not be involved in recognition of other objects. However, in trying to delineate the selectivity of pure alexia, comparing patients' performance with letters and digits is an obvious starting point, as the two types of symbol are so visually similar. If number reading is unaffected in some patients with pure alexia, this will be difficult to reconcile with theories claiming that pure alexia is the result of a low level general visual deficit.

2.4. A note on reading models

For the purpose of this dissertation, the levels of processing in visual word recognition need not be specified to any large degree. The aim is quite straightforward; to investigate the plausibility of the suggestion that visual word recognition entails a stage of processing dedicated to and specialized for word form processing (Shallice & Warrington, 1980; Warrington & Langdon, 1994), or at least

representing visual letter strings in an abstract format (Cohen et al., 2000; 2003), and whether damage to such a system may be the cause of pure alexia. However, depending on the findings in the reported studies, the levels of processing thought to be involved in visual word recognition may need to be specified, and therefore a brief mention of reading models seems appropriate.

Most cognitive neuropsychological models of word reading assume a stage of representation of the visual letter string as a whole, and this stage is either referred to as a word form system (McCarthy & Warrington, 1990), or a visual or orthographic input lexicon (Ellis, 1993; Coltheart, 1987). The levels of processing before this stage have been relatively underspecified, as these models mostly sought to describe the central reading system, and not early visual processes involved in reading. However, more recent cognitive neuropsychological reading models have included computational models specifying the early stages of written word recognition, and in general the models have become more specific regarding the computations necessary for reading (e.g., Coltheart, Rastle, Perry, Langdon & Ziegler, 2001). As pure alexia affects the early stages of visual word processing (the stages leading up to, and perhaps including a word form level) these are the processing stages of greatest interest in this dissertation. Most cognitive models now assume that early processes in visual word recognition are characterized by cascaded, interactive processing, and often take the Interactive Activation Model (IAM; McClelland & Rumelhart, 1981) as their starting point. This model assumes three levels of processing in visual word recognition: a feature level, a letter level and a word level, and information is assumed to be processed in an interactive manner. Thus, information from the feature- and letter level may feed forward to the word level before processing is completed on these levels, and activation on the word level may influence further processing on lower levels by inhibitory and excitatory feedback loops. This model is specific with regards to the computations necessary for recognition of written words, but does not specify how the suggested operations relate to visual processing of other types of visual input. The model is also not concerned with the cerebral basis of the suggested operations.

Within the broader field of cognitive neuroscience, anatomically based models of word recognition have been advanced to explain patterns of activation revealed by neuroimaging methods (McCandliss et al., 2003; Dehaene, Cohen, Sigman & Vinckier, 2005), and the validity of these models has also been investigated in patients with alexia (Cohen et al., 2004; Hillis et al., 2005). In particular, the local combinator detector (LCD) model of Dehaene et al. (2005) builds upon work within cognitive psychology and functional imaging, as well as animal models of visual object recognition, and specifies the anatomical locations assumed to be responsible for the

different computations necessary to recognize written words. Both on an anatomical level as well as with regards to the particular operations involved, this model is quite specific, but again the relation to visual processing of other visual material is not much elaborated upon. The LCD-model assumes that visual processing in both hemispheres culminates in the VWFA, where word form representations are computed, and like the IAM, the model assumes cascaded, interactive processing in visual word processing. Building in part on single cell studies in animals, this model suggests anatomically localized functional components of the reading process that are not easily distinguished on the level of resolution currently provided by functional imaging techniques (although see Vinckier et al., 2007 for an attempt). In addition, the model specifies levels or areas of neural processing that rarely, if ever, are affected in isolation by cerebral injury.

For the present purposes, it is assumed that visual word recognition, and visual object recognition in general, is an interactive process with levels of processing representing increasing specification of the visual stimulus.

3. Empirical studies

Converging evidence from patient studies, imaging studies, experimental psychology, and in some cases also animal models is important for the understanding of both cognitive processes and their neural substrate(s). When investigating the question of functional and anatomical selectivity for visual word recognition, two of these methods are particularly obvious choices, namely functional imaging and studies of brain injured patients. In the following, four empirical studies will be presented, that aimed at investigating the question of selectivity by these methods. The findings from these studies will be discussed in relation to each other as well as to the general literature about pure alexia and visual word recognition, and unresolved questions and directions for future research will be outlined.

3.1. Study I: Impaired letters but not numbers: Case MT

As mentioned above, there are two main ways of investigating the question of selectivity within cognitive neuropsychology and neuroscience: One can use imaging techniques with normal subjects, or study patients with seemingly selective deficits.

One such patient was MT (Starrfelt, 2007), who presented with alexia and agraphia following closed head injury. His deficits were very selective, in the sense that they affected reading

and writing of letters and words but not numbers. No brain lesion was visible on repeated brain scans, and thus there was no anatomical hint as to which cognitive process or mechanism was damaged. This prevented the generation of a strong hypothesis regarding whether MT's problem was mostly visual in nature, more related to motor skill, or whether it had affected a more central system for written language. As MT's ability to write numbers and draw pictures was not affected, a pure motor deficit seemed unlikely, and along the same lines of reasoning a general visual deficit seemed improbable, as he could easily identify visually presented numbers and pictures. In this way the patient presented quite a puzzle, and the first question this study raised was whether MT's pattern of performance was common and could be expected, or if he was as special as he seemed at first glance. MT's deficit resembled global alexia, in that he was severely impaired in identifying even single letters, and almost unable to read words (Binder & Mohr, 1992). However, as MT had a corresponding deficit in writing, a diagnosis of "pure alexia" did not seem to adequately describe his impairments. A brief review of the literature suggested that although it was a common belief that number reading could be spared in pure alexia, very few studies had actually investigated this in pure alexic patients. As reviewed in Section 2.4, the few studies on record suggest that number reading is commonly affected in pure alexic patients, but often not to the same degree as reading of letters and words (e.g., Albert et al., 1973, Cohen & Dehaene, 1995). The clear dissociation between letters and digits observed in MT had not been reported in patients with pure or global alexia. To the author's knowledge, the only published case study where a similar dissociation was found was reported by Anderson, Damasio and Damasio (1990): After a surgical lesion in *Exner's area* in the left premotor cortex, their patient had severe impairment in reading and writing letters and words, while her number reading and written arithmetic was spared. Given that this patient had an anterior lesion, her alexia seemed to be a very pure form of *The third alexia*, a disorder described in patients with Broca's aphasia (Benson, 1977).

Exner (1881) speculated more than a hundred years ago if the premotor area that now bears his name area could have something to do with writing, placed as it is directly in front of the cortical motor area for the hand, and above the anterior language areas. The question arising from Anderson et al.'s (1990) study was why this area would be involved in reading, and why it did not seem to be involved in the writing of numbers. As MT had no visible lesion, it remains unknown if damage to Exner's area caused his problems in reading and writing. It seems clear though, that in MT a process was disturbed that was involved in reading and writing letters but not numbers, and this selectivity needs to be explained. In general, the study of MT seemed to provide more questions

than answers. These questions relate to the possibility of cerebral specialization for written language, and by extension learned abilities, for instance: Do reading and writing rely on dedicated cerebral areas? Can these areas be specialized to a degree that they are involved in reading of letters and words, but not numbers (another learned skill)?

As it has been suggested that number reading and object recognition can be intact in patients with pure alexia (Geschwind, 1965; Warrington & Shallice, 1980; Leff et al., 2001; Gaillard et al., 2006), the following studies sought to investigate the question of selectivity in the visual domain. In general, compared to studies of writing, the cerebral specialization for reading has received most attention in the literature. This is perhaps not surprising, at least not for the functional imaging literature, as reading is more easily assessed in these studies (e.g., because of movement artefacts in writing tasks). Within the patient literature, more studies concern pure alexia than pure agraphia, and the relative purity of these disorder relates directly to the question of selectivity. With regards to reading this question concerns whether pure alexia (in some cases) affects reading only, while other visuo-perceptual abilities are left intact. In the following studies we investigated the question of selectivity for visual word processing in the visual domain, both with the use of functional imaging (PET) and in patients with pure alexia. Thus, although the study of MT also raised other questions, for instance about the association of reading of writing in his pattern of performance with letters and numbers, these questions are left to future research.

3.2. Study II: The visual what for area: A PET-study

As mentioned in the introduction, Warrington & Shallice (1980) suggested that word reading includes a stage where the *visual word form* is important. They defined this visual word form system as one which "parses (multiply and in parallel) letter strings into ordered familiar units and characterizes these units visually" (p. 109), and suggested that pure alexic patients have damage to this system. This level of processing exists in many cognitive models of the reading process, sometimes under other names like "orthographic input lexicon" (Coltheart, 1980) or "visual input lexicon" (Ellis, 1993). A more recent version of the visual word form hypothesis suggests the existence of a cerebral area responsible for computing representations of "abstract letter identities invariant for parameters such as spatial position, size, font or case" (Cohen et al. 2003; p. 1314): The Visual Word Form Area (VWFA). As mentioned above, the existence of such an area as well as the suggested name has been challenged on both theoretical and empirical grounds (Price & Devlin, 2003; 2004), and the cognitive operations to which it contributes have also been widely

discussed (Devlin, Jamieson, Gonnerman & Matthews, 2006; Hillis et al., 2005). Study II (Starrfelt & Gerlach, 2007) relates to this debate.

A brief review of neuroimaging studies of the VWFA's involvement in visual processing suggested that this area was quite consistently found activated by words or letters compared to rest or simple visual stimuli like fixation-crosses or checkerboards (e.g., Cohen et al. 2000; 2002), but not when written stimuli were compared to more complex visual stimuli like pictures of objects (e.g., Joseph et al., 2003; 2006). On this basis, we hypothesized that activation in the putative VWFA was affected by visual complexity, and in particular the degree of shape processing demanded. To test this hypothesis, we conducted a PET-study comparing activation in the putative VWFA in tasks demanding varying degrees of shape processing. We used two kinds of stimuli: line drawings and written words. One main finding was that there *is* something special about word processing in the VWFA. In a general comparison, words activated the VWFA more than pictures. Indeed, this area was activated by written words even a task that do not demand that the words are read; a colour decision task (deciding the colour of the ink the word is written in). In a corresponding colour decision task with pictorial stimuli, there was less activation in the VWFA, and the difference between activation in the two conditions was significant. However, this pattern was not quite as convincing when subjects performed a task demanding explicit recognition and categorization of the stimuli. In this task, the VWFA was still more activated by words than pictures, but the difference was no longer significant. In a third task, an object decision task with pictorial stimuli only, we found that the activation in the VWFA was higher than in any of the other tasks and conditions. This latter task places high demands on shape differentiation. In sum, in simple tasks where shape processing is in principle not necessary, the VWFA is activated more by words than pictures, but in tasks demanding shape processing, and especially when there are high demands on perceptual differentiation, the VWFA is activated by pictures as well as words.

On this basis we suggested that the cognitive process subserved by the VWFA could be *shape configuration*, the integration of shape elements into elaborate shape descriptions corresponding to objects or words. However, to fully explain our findings, another premise must be given: it seems as if word shape is processed regardless of task demands, while the process of shape configuration is more flexible for pictures depending on task requirements. This may relate to the relative automaticity with which we read (Posner, Sandson, Dhawan & Shulman, 1989), which is clearly illustrated by the Stroop effect (Stroop, 1935) where words are processed even when this is detrimental to performance. We concluded that the VWFA is not specialized for or dedicated to

reading, but rather that this area subserves the general process of shape configuration. This process is important for reading, and words seem to go through this level of processing regardless of task demands. On this basis we speculated that lesions in this area may affect reading more than visual object processing, but that patients with lesions in the VWFA in addition to reading problems, should also have deficits in tasks placing high demands on shape configuration.

Intermezzo

Based on these two studies: A patient study suggesting that reading *and* writing of letters and words can be dissociated from number reading and writing, as well as from object naming and drawing (Starrfelt, 2007), and a PET-study suggesting that the proposed visual word form area is involved not only in reading but also in object processing (Starrfelt & Gerlach, 2007), new questions emerged. These concerned whether reading can be dissociated from object naming in patients with lesions in ventral visual areas like the VWFA, and whether reading of letters and words can be dissociated from number reading in the visual domain. On a more general level, these questions relate to the ongoing debate about the cerebral specialization for reading.

Patient MT had no visible brain lesion, and therefore the cerebral basis of his deficits remains a mystery. Also, quite crude measures were used in that study, and more subtle deficits may have gone unnoticed. The observed dissociation is still quite impressive, there is no doubt that MT was infinitely better at reading and writing numbers than letters, a point that needs to be explained even if he should have had more subtle deficits in other areas. In the PET-study, our findings strongly indicate that the VWFA is involved not only in word reading but in object processing, and on this basis we suggested that the cognitive operation performed in this area was shape configuration. But imaging studies can only shed light on areas associated with normal performance, and cannot delineate which areas are *critical* for a given cognitive process. Thus it is possible that although the VWFA is activated by both words and pictures in our study (and others), this area is only critical for word reading and not object processing. If so, lesions in this area should give rise to reading problems but, depending on the selectivity of the lesion, leave processing of other objects and perhaps even numbers intact.

Thus we wanted to address some of the questions raised by the first two studies in patients with cerebral lesions. Studying patients with pure alexia was the obvious choice, both because their deficits *are* by definition pure, and because the critical lesion in pure alexia is thought

to involve the visual word form area (e.g., Cohen et al., 2003; 2004; Leff et al., 2006). As mentioned in the introduction, the stimuli one chooses to compare are of great importance both in patient studies and in neuroimaging of cognitive processes, especially when the aim is to characterize the selectivity of a disorder, or in the case of functional imaging a cerebral area. In the following studies we aimed to apply both sensitive measures and sensible stimulus comparisons. Based the study of patient MT (Starrfelt, 2007) one obvious choice was to compare letter and digit perception in pure alexic patients. This was desirable because few studies have compared pure alexic patients' performance with letters and digits, and it therefore remains uncertain whether dissociations like the one observed in patient MT can arise in visual perception. Because letters and digits are visually very similar, preserved digit identification with impaired letter identification would be quite convincing evidence that pure alexia affects alphabetical material only. Based on the finding that line drawings of objects activated the putative VWFA (Starrfelt & Gerlach, 2007), we also wanted to investigate whether pure alexic patients are impaired with this stimulus category.

In an earlier study of alexia due to a subtle visual field defect (Habekost & Starrfelt, 2006), we were able to characterize the patients' reading deficit in detail by using classical psychophysical experiments and analysis based on a Theory of Visual Attention (TVA; Bundesen, 1990; Bundesen, Habekost & Kyllingsbæk, 2005). In general, the TVA-framework has proven effective for characterizing visual attention deficits after different types of brain damage (Duncan et al., 1999; Peers et al., 2005; Finke, Bublak, Dose, Müller & Schneider, 2006). TVA-based patient studies have been shown to be highly sensitive, as they can reveal subclinical deficits not evident on standard clinical tests (Habekost & Rostrup, 2006; Habekost & Starrfelt, 2006), and highly specific, in that specific components of visual attention can be singled out in TVA-based analyses (Duncan et al., 2003; Habekost & Rostrup, 2007). In addition, TVA-parameters relating to visual attentional capacity can be assessed for different stimulus types, and thus the generality of visual deficits, for example whether they are specific to alphabetical material or not, can be investigated within this framework. TVA modelling enables performance on simple psychophysical tasks (single stimulus report, whole report, partial report) to be analyzed into different functional components. For example, the whole report paradigm measures two central parameters of visual capacity: The capacity of visual short term memory, *K*, and the speed of visual processing, *C*. The *K* parameter represents the ability to perceive multiple items in parallel (the apprehension span). The *C* parameter reflects the efficiency of visual recognition, which may be tested for different stimulus types and using displays of either multiple or single items. These two TVA-parameters are of

particular interest to investigations of pure alexia (and peripheral alexias in general), as different theories predict different patterns of impairment in processing speed and visual apprehension span. Indeed from several theories of pure alexia, direct predictions can be made about the relative affection of *K* and *C* for different stimulus types (see below).

To my knowledge, only one previous study have used TVA-based analysis in the context of pure alexia (Duncan et al., 2003), and as the current work owes much to this particular study, a detailed presentation seems appropriate. The aim of Duncan et al.'s (2003) study was to compare the performance of one patient with *dorsal simultanagnosia* with that of a patient with pure alexia, or in their terms *ventral simultanagnosia.* They wanted to investigate whether these disorders are, as their names imply, characterized by a deficit in perceiving multiple items simultaneously, which in TVA-terms would be defined as a reduced *K*. This is of particular interest here, since some theories of pure alexia suggest that a deficit in simultaneous perception is the underlying cause of this disorder (e.g., Kinsbourne & Warrington, 1962; Farah, 1990), hence the name ventral simultanagnosia. Indeed, Duncan et al. (2003) did find a reduction in visual apprehension span in their pure alexic patient, but importantly the patient could perceive more than one item at a time, indicating some ability for simultaneous perception of visual stimuli. Processing speed, on the other hand, was severely reduced, leading Duncan et al. (2003) to conclude that the main deficit in pure alexia was not in simultaneous perception, but rather a general reduction in processing speed. The same pattern also characterized the patient with dorsal simultanagnosia. However, as dorsal simultanagnosics (including the patient reported by Duncan et al., 2003) can read words without resorting to a letter-by-letter strategy (Baylis, Driver, Baylis & Rafal, 1994; Vinckier et al., 2006) there appears to be another deficit present in ventral simultanagnosia, one that prevents whole word reading. In the words of Duncan et al. (2003, p. 699): "In word perception, it is commonly presumed that learning has bound component letters into a single familiar object, releasing them from the competition that unrelated letters would suffer (Sieroff & Posner, 1988). For (…) dorsal simultanagnosics, we would suggest that this binding remains intact." For ventral simultanagnosics, they suggest that the reduction in processing speed is "complicated by an additional deficit in word recognition itself. Because of this deficit, even letters in familiar words suffer some of the same processing competition as unrelated display elements".

One potential problem with Duncan et al's (2003) study is that only letters were used as stimuli in their experiments. As their alexic patient had slight letter identification difficulties even in a paper-and-pencil test, the results leave open the question of whether the reported pattern

of deficits characterize the patient's visual perception in general, or merely his perception of letters. In the following studies, we aimed to overcome this problem by including digits as stimuli in addition to letters. Variations of the TVA parameters of *K* (apprehension span) and *C* (processing speed) for the two kinds of stimuli (letters and digits) relate directly to the main hypotheses of pure alexia mentioned in the introduction: The simultanagnosia hypothesis should predict that *K* is impaired for all stimulus types, whereas *C* may be normal in single-stimulus situations. Instead, if a general visual recognition deficit underlies pure alexia, *C* for different object types should be affected also with single stimuli. Finally, if the problem is specific to letter perception, then *C* should be reduced for this particular stimulus type, but perception of other stimuli may be normal, including the ability to recognize multiple items at the same time (*K*).

Duncan et al. (2003) suggested that the lack of integration of letters into words may be an inherent feature of pure alexia, and that because of this deficit, letters in words suffer some of the same processing competition as unrelated letters. That is, in pure alexia letters in words may be processed in the same highly capacity limited way that characterises normal processing of unrelated letters. The suggestion that "learning has bound component letters into a single familiar object" (Duncan et al., 2003; p. 699) may resemble the word form hypothesis of pure alexia, the idea that this reading disorder arises because of a disturbance in a word specific system (e.g., Warrington & Shallice, 1980; Cohen et al., 2004). However, as argued by Starrfelt & Gerlach (2007), this binding may perhaps be achieved by a more multi-purpose process, for instance shape integration. Either way, it seems plausible that in comparison to dorsal simultanagnosia, there may be an additional deficit in pure alexia as these patients do not seem to perceive a word like one object, but commonly process it in a letter-by-letter fashion (Behrmann, Plaut & Nelson, 1998; Rayner & Johnson, 2005). In Study III we attempted to address this question.

3.3. Study III: Visual processing in pure alexia: Case NN

Starrfelt, Habekost and Gerlach (2008) reports a case study of a patient (NN) who suffered from pure alexia after haemorrhage in the posterior part of the left hemisphere. We explored the possible selectivity of his disorder in a series of experiments using letters, numbers, words and pictures as stimuli. Based on the two previous studies, as well as the ideas mentioned above, two lines of investigation were set up:

First we aimed to address the question of selectivity by comparing NN's performance with letters and digits in two experiments. Recognition of single letters and digits in the central

visual field was tested with a single item report task, and visual apprehension span and peripheral processing speed was measured in a whole report experiment with letters and digits (in separate conditions). The results were analysed within the framework of TVA (Bundesen, 1990). Furthermore, we investigated NN's letter reporting ability in an experiment where both words and nonwords were used as stimuli (a word superiority experiment), to test the hypothesis put foreward by Duncan et al. (2003) that patients with pure alexia perceive letters in words in the same (highly capacity limited) way that characterizes normal perception of unrelated items. Secondly, using comparatively simpler but yet quite sensitive measures, we characterized NN's picture processing with computerized tests measuring reaction times (RTs). NN performed an object naming task, and an object decision task with outline drawings and chimeric nonobjects, a task we found to activate the putative visual word form area (Starrfelt & Gerlach, 2007). Furthermore, based on a suggestion that pure alexic patients may show disproportional difficulties in tasks with few perceptual cues to guide integration (Sekuler & Behrmann, 1996), we included an object decision task with fragmented drawings, a task that places very high demands on shape integration and perceptual differentiation. NN's performance in these tasks was compared to normal controls.

Two important findings emerged from this second line of investigation: First, NN's performance was within the normal range on the object naming and object decision tasks with outline drawings. This was somewhat surprising, as pure alexic patients have been found to be impaired in picture naming, at least with complex pictures (Behrmann, Nelson & Sekuler, 1998). In particular, his performance in the object decision task was unexpected, as this test is fairly difficult and demands rapid and effective differentiation between objects and nonobjects. Thus, NN suffered from a particularly pure form of alexia compared to other patients in the literature, which makes his performance in the other experiments even more interesting. In the object decision task with fragmented pictures, NN's performance was qualitatively different from controls: His error rate, as well as his RTs to nonobjects were on the same level as controls, but his RTs to real objects were elevated compared to the control group. We suggested that this may reflect a subtle deficit in shape integration that becomes evident in conditions where visual input is degraded and there are few cues to guide the integration process (cf. Sekuler & Behrmann, 1996).

With regards to the TVA-based assessment, NN's processing speed was significantly reduced for single stimuli presented at fixation: His ability to recognize single letters was severely impaired, and he was also impaired in single digit recognition, although not to quite the same degree. Further, the whole report experiment revealed that NN's visual apprehension span was

reduced for both letters and digits, and he was able to encode a maximum of three items simultaneously. Surprisingly, NN's processing speed was within the normal range in the peripheral part of the visual field. However, while controls performed much better with central stimuli, that is, their processing speed was higher for single items presented at fixation compared with the more peripheral presentation in the whole report experiment, this pattern was not evident in NN. His processing speed was at about the same level in both conditions, indicating an impairment of shape perception in the central visual field, resembling a form of foveal amblyopia. As shape perception in the central visual field is extremely important in reading (Rayner & Bertera, 1979), this deficit may be of particular importance to NN's alexia.

The word superiority experiment provided more mixed findings. In an overall analysis, NN showed a significant word superiority effect, that is, he consistently reported more letters from words than from nonwords. However, he performed no different with pronounceable nonwords than with words. This pattern was not found in controls, who showed a significant word superiority effect, but no significant effect of pronounceability. In addition, the number of letters NN could report in this experiment, regardless of whether the stimulus was a word or a nonword, was significantly reduced compared to controls. It is notable that NN could not exceed this visual apprehension span when reporting letters from real words. In normal reading, and in dorsal simultanagnosia, letter report from words can be superior to the visual apprehension span as letters in words are not processed as independent items. However, while NN is clearly impaired in reporting letters from briefly presented words and nonwords, the experimental setup did not allow us to decide whether reduced processing speed or reduced apprehension span (or both) were responsible for his performance in this task.

What this makes clear, however, is that the rapid integration of letters into words is either absent or severely impaired in NN. This resembles his performance with the fragmented pictures, where a deficit in shape integration also seems to be present. We suggest that the breakdown of this integration process contributes significantly to NN's alexia, as this reduces words to their constituent parts (letters). This makes processing of letters in words susceptible to limitations in visual attentional capacity, which could explain why a reduced span of apprehension can have an effect on reading in pure alexia, while it does not seem to affect word reading in patients with dorsal simultanagnosia. In addition to this integration deficit, NN's recognition of single letters is impaired, an impairment that would also be expected to contribute to his alexia. In

sum, even in a particularly pure case of pure alexia, we find evidence of at least two separable deficits, of which neither is selective to alphabetical stimuli.

3.4. Study IV: Too little, too late: A multiple case study of visual processing in pure alexia

The results from the case study of NN (Starrfelt, Habekost & Gerlach, 2008) suggest that recognition of line drawings can be preserved in pure alexia. This has been reported before (e.g., Gaillard et al., 2006), but only with regards to naming accuracy and not RT. As word reading in pure alexia is commonly slow but accurate, and deficits in visual integration can affect naming RTs without affecting accuracy (Gerlach, Marstrand, Habekost & Gade, 2005), it seems important to include measures of RT in non-reading tasks as well. In spite of preserved recognition of outline drawings, processing of single letters and digits was impaired in NN, and his visual apprehension span was reduced for both letters and digits. In Study IV, we investigated the generality of these findings in four patients with relatively mild pure alexia (Starrfelt, Habekost & Leff, 2008), mainly by employing the same methods as in Study III (Starrfelt, Habekost & Gerlach, 2008). Processing speed and apprehension span for letters and digits was measured using single item report and whole report paradigms, and TVA-based analysis. In addition we included a naming task and an object decision task with outline drawings. The patients' performance on these tests was compared to normal controls.

The main findings in this study are strikingly similar to those reported in Study III (Starrfelt, Habekost & Gerlach, 2008): All patients were severely impaired in single letter recognition compared to controls. Single digit recognition was also impaired in all patients. All four patients had significantly reduced visual apprehension span, and this was valid for both letters and digits. Processing speed in the whole report experiment was reduced in the patient group as a whole compared to controls, but this did not reach significance when comparing the individual patients to the control group. One patient in this study had pure alexia without a visual field defect. His performance in the whole report experiment could therefore be assessed in both visual fields, and his performance was very similar in both sides. This finding is important, as most pure alexic patients have field defects affecting the right visual field, and thus their visual processing capacity must in many cases be evaluated by presenting stimuli to the left visual field only. With regards to performance with pictorial stimuli, all patients were accurate in naming of line drawings, while their RTs were elevated compared to controls. In the object decision task, all patients were as accurate as controls (or better). Two patients also had RTs within the normal range on this test, while two

patients' RTs were elevated compared to controls. The four patients in this study had lesions of varying size and location within the posterior left hemisphere. The only region affected in all patients was the left fusiform gyrus. This supports the suggestion that this area is of particular importance in reading.

In sum, we find that single letter and single digit recognition is impaired in four patients with pure alexia, and that visual apprehension span for both letters and digits is affected also. In addition, all patients in this study showed evidence of subtle deficits in object naming or recognition. This suggests that even mild pure alexia is not a deficit selective for or restricted to alphabetical material. In addition, a deficit in simultaneous perception does not seem to account for the patients' pattern of performance, as they are all clearly impaired with single stimuli also. Rather, these findings suggest that pure alexia is a visual disorder that affects recognition of letters, words and numbers as well as pictures. We suggest that the reduced recognition efficiency in the centre of the visual field, taken to reflect impaired shape perception, is the most important factor in causing the patients' reading problems.

3.5. Summary of studies III and IV

There are several interesting aspects in the patterns of performance observed in the pure alexic patients reported here (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), both with regards to similarities and differences between patients. The most striking commonalities between patients in both studies were: i) Impaired recognition of single letters and digits presented at fixation; ii) Reduced visual apprehension span for both letters and digits, and iii) Impairment in picture naming or recognition tasks. With respect to the latter, the patients showed varying degrees of impairment in picture recognition and naming, and in one patient this deficit was only evident in a difficult task with fragmented drawings. Starrfelt, Habekost and Gerlach (2008) suggested that two possibly separable deficits contributed to NN's alexia: Impaired letter recognition, due to a general deficit in shape perception, and impaired shape integration. Neither deficit was assumed to be selective to words or letters. We hypothesized that (pure) alexia may arise because of either one of these deficits, as both identification of letters and integration of letters into words is necessary for fluent reading. For visual apprehension span to affect word reading, a deficit in the integration of letters into words should be present. Based on this idea of two separable deficits, one could have expected larger differences between the reported patients, but rather we find that the patients show a remarkably similar pattern of performance. All five patients were impaired with single digits as well

as single letters, all showed reduced visual apprehension span for both types of stimuli, and all showed signs of impairment with pictorial stimuli. In addition, all five patients had lesions affecting the left fusiform gyrus, including the region referred to as the visual word form area. In the following, these results will be discussed in relation to Studies I and II (Starrfelt, 2007; Starrfelt & Gerlach, 2007), as well as the general literature concerning visual word recognition and pure alexia.

4. Findings and further questions

4.1. Letter recognition in (pure) alexia

A deficit in single letter recognition was evident in all the reported pure alexic patients (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), and even more clearly so in patient MT (Starrfelt, 2007). It has been suggested that a deficit in letter identification is present in all patients with pure alexia (or LBL-reading; Behrmann, Plaut & Nelson, 1998), and that this deficit may in itself explain the patients' reading problems (Behrmann & Shallice, 1995). Behrmann, Plaut and Nelson (1998) suggested an explanation for LBL-reading based on the Interactive Activation Model (IAM, McClelland & Rumelhart, 1981; Seidenberg & McClelland, 1989), mentioned in the introduction. In a cascaded system like the IAM, partial information about a stimulus can be passed on to higher levels in the system, and since the system is interactive, activation on superior levels will feed back to preceding levels. For reading, this means that partial or degraded information about letters and letter features may feed forward to the word level, which by feedback loops may inhibit or strengthen representations on the feature and letter level. Behrmann, Plaut and Nelson (1998) suggested that the important deficit in LBL-reading lies either at the feature level, or between the feature level and the letter level. This results in weak activation on the letter and word levels, activation not sufficient for explicit word identification. To enhance letter activation and allow word identification, letters are processed sequentially (letter-by-letter).

In this way the letter processing deficit present in the reported pure alexic patients (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008) may explain their word reading pattern, their word length effects. Similarly patient MT's (Starrfelt, 2007) severely impaired letter recognition abilities may explain why he was almost unable to read words. However, this does not explain *why* these patients have a deficit in letter recognition. Behrmann, Plaut and Nelson (1998) pointed out that the letter identification deficit in LBL-reading may be attributed to an even more fundamental perceptual impairment, and at least in the pure alexic patients presented here a

more general deficit seems to be the present, as they are all impaired in number reading also (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008).

A recently suggested explanation for the word length effects observed in pure alexia (or LBL-reading) is the *letter confusability account* mentioned in the introduction. According to this hypothesis, the word length effect in LBL-reading arises because of an abnormal sensitivity to letter confusability in word reading (Fiset et al., 2005; 2006). When letter confusability is controlled for the word length effect "disappears": RTs are similar for words of different lengths if the summed confusability of the constituent letters is the same in the two conditions (Fiset et al., 2005). As letter confusability did not have impact on the patients' RTs to single letters in this study, Fiset et al. (2005) argued that the effect arises when attention is distributed over a whole word. In some ways this hypothesis resembles the simultanagnosia hypothesis, as it argues for a deficit that is only present when multiple letters must be perceived simultaneously. In the pure alexic patients reported here, we find that single letter recognition is impaired (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), and thus it seems unlikely that the distribution of attention should be the main cause of our patients' reading problems. In addition, since our patients are also impaired in single digit recognition, a letter specific impairment cannot explain their performance. However, in extending the letter confusability account, Fiset, Gosselin et al., (2006) suggested that LBL-readers have reduced sensitivity to the spatial frequencies optimal for letter and word recognition. They investigated this hypothesis in a group of normal subjects by presenting them with high-pass filtered, low contrast words. In this condition, the performance of their subjects very closely resembled that of a letter-by-letter reader. In addition, Fiset, Gosselin et al. (2006b) showed that the effect of letter confusability on RTs was absent when this patient read high passed filtered words, while the confusability effect was exaggerated with low-pass filtered words. Thus, they suggested that the crucial deficit in LBL-reading is a loss of the ability to use the optimal spatial frequency for reading. Effects of letter confusability arise when parallel letter processing must rely on lower spatial frequencies, and to overcome this problem LBL-readers attend serially to single letters to extract higher spatial frequencies.

This loss of the ability to use spatial frequencies important for reading may well be the "general visual deficit" suggested to be at the core of pure alexia (Farah & Wallace, 1991; Behrmann, Nelson & Sekuler, 1998; Sekuler & Behrmann, 1996). Fiset, Gosselin et al. (2006b) argue that this deficit, although general, involves "spatial frequencies too high to be a real nuisance for other classes of objects" (p. 1472), although they mention complex natural objects as a possible

exception. Also, they consistently claim that the letter confusability effect arises only when parallel processing is demanded, and that attention to single letters abolishes this effect. However, an account of pure alexia (or LBL-reading) should also explain the deficit in single letter processing evident in these patients (Behrmann, Plaut & Nelson, 1998; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), a deficit also apparently present in Fiset et al.'s (2005) patients judged by their RTs in letter naming. Although it may not give rise to confusability effects when letters are presented in isolation, the suggested reduced sensitivity to "medium range spatial frequencies" may still impair single letter processing. If so, then our findings of impaired processing of both single and multiple letters and digits (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), and perhaps also the patients deficits in object recognition, may be attributed to the same underlying deficit. There is no a priori reason to expect impairment in the use of "the optimal spatial frequency band for letter and word recognition" (Fiset, Gosselin et al., 2006, p. 1466) to have a differential impact on letter and digit processing, neither on report from single or multiple displays of the same stimuli. However, this should be formally tested, for instance by assessing normal subjects' performance with single and multiple letters and digits using varying degrees of spatial filtering of the stimuli. Investigating the impact of letter confusability on single letter recognition in both normals and alexic patients may also be done in psychophysical paradigms like the ones used in our TVA-based investigations, as this may provide more sensitive measures than RTs. It is not unlikely that an effect of confusability on single letter recognition would be found in pure alexic patients (or LBL-readers) with more sensitive measures, and it is also possible that high pass filtering of single letters may induce confusability effects in normal subjects.

Fiset, Gosselin et al. (2006) suggest the following explanation for the underlying deficit in LBL-reading, one that they admit is highly speculative at this point: Visual areas in the left hemisphere have been suggested to be of particular importance for extraction of visual information from medium and high spatial frequencies, and this could potentially explain both: i) Why reading relies on left hemisphere processing more than right hemisphere processing, as important information about letters and words are provided by these spatial frequencies, ii) Why damage to posterior areas in the left hemisphere disrupts the reading process, and gives rise to pure alexia. In addition, hemispheric differences may also explain why the right hemisphere, which is more sensitive to low spatial frequencies, fails to support normal reading in patients with pure alexia. The parallel processing that gives rise to effects of letter confusability in LBL-reading is assumed to be supported by right hemisphere mechanisms that depend mainly on low spatial

frequencies, while the serial attention to each letter (or the most confusable ones) is supported by areas in the left hemisphere sensitive to very high spatial frequencies.

While this account is much more specific than others claiming that a low level deficit is the cause of pure alexia or LBL-reading, more research is needed to evaluate its potential explanatory power. For instance, the suggested left hemisphere area sensitive to spatial frequencies important for reading must process input to both visual hemifields and cerebral hemispheres, as hemianopic patients with posterior left hemisphere lesions do not exhibit word length effects like those observed in pure alexic patients. Although patients with visual field defects affecting foveal vision commonly have reading problems, and even show slight word length effects in reading (Zihl, 1995; Leff et al, 2001), there is nothing to suggest that they cannot process spatial frequencies important for reading in their intact visual field.

It has been suggested that if pure alexic patients perform accurately on tests of letter naming, their deficit should not be attributed to a general visual deficit, as patients with right hemisphere lesions may have severe perceptual deficits and still be able to read normally (Warrington & Langdon, 2002). The results presented here suggests that accuracy in letter naming is not a sensitive measure of letter recognition, and that visuo-perceptual deficits should be examined carefully in pure alexic patients as subtle deficits may be revealed by more sensitive measures (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). While there is no independent point in revealing deficits that have no impact on everyday performance, there is a point in doing so if a characterization of these deficits can shed light on the nature of the patients' reading problems. Strategies employed in attempted rehabilitation of pure alexia will differ depending on whether the reading deficit arises on a level specific to letter or word processing or if it is caused by a general impairment in visual processing. For this reason, the contributing factors should be carefully assessed in individual patients. Interestingly, Fiset, Gosselin et al. (2006b) note that their LBL-reader felt improvement of his reading ability after reading more than a hundred low pass filtered words, and suggest that rehabilitation strategies may take advantage of this. This suggests that the relation between spatial frequency information and both normal and pathological reading deserves further investigation, as this could potentially contribute substantially to our understanding of visually based reading deficits, and the mechanisms through which they may be ameliorated.

4.2. Object recognition in pure alexia

One question that has kept surfacing in the debate of the purity of pure alexia is whether object recognition or naming can be intact in this disorder. This has been related to the larger debate of whether or not the suggested visual word form area in the left mid-fusiform gyrus contributes to recognition of other visual material than words (Price & Devlin, 2003; McCrory, Mecheli, Frith & Price, 2005; Devlin et al, 2006; Gaillard et al., 2006). In our PET-study comparing words and outline drawings (Starrfelt & Gerlach, 2007) we found that activation in the VWFA depended on task demands especially for pictures, and that activation in the VWFA was greater during an object decision task with pictures than during categorization of words. Thus we hypothesized that the VWFA may contribute to the process of *shape configuration*; the integration of shape elements into elaborate shape descriptions corresponding to whole objects or words. We interpreted the observed pattern of activation as reflecting a general perceptual process, not a process specific to reading. At the same time we did find that words activated this region more than pictures, particularly in tasks where identification of the stimulus was not necessary for performance, and we attributed this effect to the relative automaticity with which we read (Stroop, 1935; Posner et al., 1989).

Object decision tasks are thought to yield relatively pure measures of visual object recognition compared to picture naming which may be slowed or error prone due to post-perceptual language processes. At the same time the object decision task employed in our studies (Starrfelt & Gerlach, 2007; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008) where nonobjects are constructed by exchanging parts of real objects, is a fairly difficult task that demands subtle discriminations between objects and nonobjects. Although the VWFA was activated in normal subjects performing this task, some patients with lesions in this region perform within the normal range both with regards to errors and RTs (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). Indeed, all the reported patients perform well in this task compared to what one would have expected if the observed activity in the VWFA reflected a process necessary for picture recognition. However, four of the reported patients were slow in naming pictures (Starrfelt, Habekost & Leff, 2008), and this could potentially be explained by hemispheric differences: The right hemisphere may be capable of extracting sufficient information about pictures or line-drawings to aid recognition, while naming (and reading) demands left hemisphere processing. Indeed, the PET-study (Starrfelt & Gerlach, 2007) indicated that the right hemisphere homologue to the VWFA was activated more by pictures than words, although this was not formally analyzed. An alternative explanation might be that subtle discrimination between visual

objects is dependent on left hemisphere areas in close proximity to areas important for visual word recognition (whether these are specific to this process or not). Two patients were impaired on the object decision task also, while their lesions affected the left hemisphere only, and this may suggest that the latter explanation is to be favoured. This may imply that occipito-temporal regions in the left hemisphere are of a certain importance for fast and efficient object recognition and in particular object naming, while these regions are not essential for recognition success or naming accuracy.

One important question arising from these observations is why patients with pure alexia rarely complain about other visuo-perceptual problems. Of the five pure alexic patients reported here (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), none complained of any cognitive deficits but their reading problems. Even though our investigations revealed that they are impaired with digits and drawings also, impairments we attribute to general deficits in visual perception, this goes rather unnoticed by the patients. Their reading problems, on the other hand, are experienced as a great handicap. This may relate to the suggestion of Sekuler & Behrmann (1996) that reading is a perceptual condition stripped of intrinsic cues to guide integration of the percept. This characterizes reading in general, while it does not characterize object recognition in the three dimensional visual world outside the laboratory. Although the patients' RTs in picture naming were elevated, such a problem may be less obvious in everyday life than the corresponding pattern (slow but accurate) in reading. In visual agnosia, real objects are often recognized better than photographs of objects, which again are recognized better than line drawings (Farah, 1990), suggesting that line drawings present a greater perceptual problem than real objects or photographs. A similar effect has also been shown in normal subjects, where naming latency decreases when colour and texture is added to simple line drawings (Rossion & Portois, 2004). Thus, the impairment observed in our patients in the naming and object decision tasks (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008) possibly reflects a real perceptual problem, but one that may not be very noticeable when cues to aid object recognition are present. Reading, on the other hand, is probably done in much the same way regardless of whether the word is presented on a computer screen, in a text, or on a streetsign. Thus, although the elevated RTs observed in the naming and object decision tasks in all probability reflect a deficit in visual processing, the impact this deficit has on reading may be more evident both to the patients and their environment. This could be further investigated by examining pure alexic patients' performance with photographs compared to line drawings, as the deficit in object recognition may be even less evident with more natural stimuli. However, this also points to the importance of assessing pure

alexic patients' object recognition abilities with challenging tasks to address the nature of the visual deficit(s) possibly contributing to their reading problems, as discussed above.

4.3. Number reading in alexia

The study of MT (Starrfelt, 2007) inspired much of the current work, and one of the questions arising from that study was whether the observed dissociation between processing of letters and digits may arise in visual perception. Thus, an important issue was whether number reading is affected in pure alexia or whether, in some cases, it can be preserved. A review of the literature suggested that it was commonly assumed that number reading could be preserved in pure alexia, a notion that probably dates back to Dejerine (1892) who claimed that number reading was preserved in his pure (or global) alexic patient Monsieur C. This conception was upheld by Geschwind (1965), who stated that "the reading of numbers is also frequently preserved in these cases - in Dejerine's case number reading was perfect". Dejerine's claim was based on the patient's ability to write down and add two-digit numbers. Landolt, the ophthalmologist who examined Monsieur C, told a different story: According to his description, Monsieur C was unable to read multidigit numbers as such, but could merely name their constituent digits (112 was read 1-1-2). Only after writing these digits down, could the patient name the multidigit number (Bub et al., 1993). This pattern of performance, reading the number digit-by-digit, resembles how many pure alexics read words (i.e. by using a letter-by-letter strategy), and strongly suggests that number reading was not normal in this patient. However, his number identification skills seem to have been better preserved than his reading and letter identification, as he could not name one single letter from visual input only.

As briefly reviewed in section 2.3., there are reports of preserved number reading in pure alexia, although specifications about assessments are sparse (Luhdorf & Paulson, 1973; Leff et al., 2001). In more detailed reports the trend suggests that number reading is impaired in pure alexia, although not necessarily to the same degree as letter identification (e.g., Albert et al., 1973; Cohen & Dehaene, 1995). This is supported in our studies, where we find that all patients are impaired in recognizing even single digits, while some patients fare better with single digits than single letters (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). In some patients with alexia *with* agraphia, number reading has been quite convincingly demonstrated to be preserved (Anderson et al., 1990), a dissociation also shown in patient MT (Starrfelt, 2007). The opposite pattern, impaired number reading and preserved letter reading, has also been described

(Cipolotti, 1995), indicating that the two symbol types may be processed by dissociable systems at some levels of processing. The current study suggests that this dissociation is unlikely to arise in visual recognition processes, while it remains unresolved why central disturbances can affect word and letter reading and leave number reading intact (although see below).

There is a quite substantial literature concerning number processing both in normals and in brain injured patients (e.g., Feigenson, Dehaene & Spelke, 2004; Hubbard, Piazza, Pinel & Dehaene, 2005; Gelman & Butterworth, 2005) which on some points overlap with studies of language and reading. For instance, theoretically challenging dissociations between reading of numbers and number words compared with non-number words have been reported (Butterworth, Capelletti & Kopelman, 2001; Denes & Signorini, 2001), and these dissociations are thought to arise on a semantic level. It is possible that patient MT (Starrfelt, 2007) was a very pure case of a deficit resembling that of Butterworth et al's (2001) patient, whose reading of numbers and number words was preserved while reading of non-number words was severely impaired, and in retrospect it would have been interesting to see how MT would have performed with number words. Also, while we failed to find a clear dissociation between letter identification and number reading in our pure alexic patients (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), further research is needed to clarify whether such a dissociation between letter and digit recognition could arise in the visual domain. As mentioned above, some pure alexic patients' number reading abilities seem *relatively* spared in comparison with their word reading skills, and this could point to some degree of dissociation between visual recognition of letters and digits.

As mentioned in the section on object recognition, patients with pure alexia rarely report difficulties with recognizing objects or numbers, and this is also true for the patients reported here (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). Usually, numbers are not presented in a glance as in our experiments, but rather remain visible during reading, and thus subtle deficits in single digit recognition may not be obvious in everyday life. Also, in reading multidigit numbers, at least numbers that exceed two digits, normal subjects show a "number length effect" on reaction times, indicating that they parse the number into its constituent digits (Brysbaert, 2000). This may not be true for familiar numbers like dates (e.g., 1987) or brand names (e.g., 737) (Alameda et al., 2003). As our patients were able to recognize single digits accurately, albeit more slowly than controls, they should be able to read multidigit numbers without resorting to an abnormal strategy. This may perhaps explain the observation that pure alexic patients read multidigit numbers normally when presented in free vision (Leff et al., 2001). For word reading this

is different, as letters in words are normally processed fast and in parallel, with little or no effect of word length on reaction times (Weekes, 1997; see also Cumming et al., 2006; Pelli et al., 2006). Thus a serial strategy or even general slowness on a letter level will result in noticeable reading problems. A way to test this would be to present pure alexic patients and normal subjects with familiar and unfamiliar numerical stimuli (e.g., contrasting their reading of 1945 compared to 4591). One could expect that pure alexic patients would show a "number length effect" even with familiar numbers, while this effect would be minimal in normal subjects. Both groups should show an effect of number length on the reading of unfamiliar numbers.

4.4. Late experience alters vision?

Throughout this dissertation, it has been assumed that letters and digits are processed in a similar manner in the early stages of visual perception. It has also been assumed that a pre-lexical deficit in letter recognition should affect digits in the same way. However, although letters and digits are similar in form, they do differ on some counts, for instance their semantic content, as evidenced by the dissociations mentioned above (e.g., Butterworth et al., 2001). Digits refer to a concrete amount and are often associated with something as concrete as the fingers. Letters on the other hand refer only to sounds and in most instances carry no meaning by themselves, while together they can form highly meaningful units. This could make letters more difficult to identify in isolation than digits. On the other hand, most of us have significantly more encounters with letters and words than with numbers, which could perhaps cause letters to be processed more easily than digits. However, our control data did not suggest any difference between normal processing of single letters and digits (Starrfelt, Habekost & Leff, 2008).

A line of studies by Polk and Farah (1995; 1998; Polk et al., 2002) investigated the processing differences between letters and digits, and how these relate to environmental factors. The essence of their suggestion is that letters generally occur with other letters in the environment, and thus by mechanisms of Hebbian learning come to be processed by a relatively specialized brain area. Digits on the other hand, occur less frequently in the environment, and often occur with letters or other symbols. Therefore a specialized area for digit processing is less likely to arise, and digits will be processed in a more distributed manner also within the letter area. If the lesion causing pure alexia affects an area relatively specialized for letters, but also contributing to digit processing, then number reading could be affected to a lesser degree that letter reading in this disorder, just as some reports indicate (Albert et al., 1973; Cohen & Dehaene, 1995). The specialization suggested by Polk

and Farah (1995; 1998) is based on learning, and the degree of specialization or selectivity is assumed to vary between individuals depending on experience with letters and digits.

As patient MT's (Starrfelt, 2007) pattern of performance seemed so peculiar (and still does), it seemed appropriate in that context to comment on individual differences in learned abilities like reading, differences that may also be reflected on a cerebral level (Polk & Farah, 1995; 1998). Reading is a skill that varies between individuals; both with regards to how much they engage in reading, how they learned the skill to begin with, as well as with regards to the specific alphabet they read. These factors may affect both the organization of the reading process in the brain as well as the strategies available to compensate for loss of reading ability. Polk & Farah (1995) suggested that "Late experience alters vision", and as mentioned in the introduction, learning to read must alter the functional architecture of the brain in some ways. Therefore one should be cautious when drawing conclusions about the organization of the reading process based on (single) case studies, as observed reading performance might differ considerably subsequent to quite similar brain lesions, and similar symptoms may arise due to lesions in different localizations. In this light it is intriguing how similar the five reported pure alexic patients are (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). Granted, they vary in degree of impairment, but within a fairly limited range. This suggests that there are strict limitations on the ways learning to read can alter the brain, and may even suggest some form of specialization within the ventral visual stream (cf. Cohen et al., 2002). Alternatively it may merely reflect that visual deficits affect visual word recognition in a predictable way.

So far, it has been argued against selectivity for word processing in the visual domain. Rather, we have shown that the visual word form area is activated by other stimuli than words (Starrfelt & Gerlach, 2007), and that even mild pure alexia can probably be attributed to a general deficit that affects visual processing of other classes of stimuli than letters and words (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). Together these studies suggest that although ventral visual areas including the VWFA are of particular importance in word reading, and although a reading problem is the only notable deficit in pure alexia, this does not demand an explanation of cerebral specialization or selectivity for visual word recognition. However, before concluding to firmly, another specialization hypothesis should be addressed. With her notion of *specialization within specialization,* based in part on the studies of letter and digit processing mentioned above, Farah (2004) has provided a frame within which the pattern of performance observed in our patients could be explained. She has suggested that depending on lesion size and

location in relation to the specialized areas for shape and letter processing "pure alexics would be expected to have a visual impairment for rapid encoding of multiple visual shapes, with varying degrees of orthography specificity" (p.57). It should be noted, that although Farah (2004) specifies the learning mechanism involved in creating a specialized area for reading, her account does not differ to any large degree from other theories suggesting specialization (Cohen et al., 2002; Dehaene et al., 2005). There is, to my knowledge, no account of visual word recognition that claims that a specialized area is present from birth or automatically develops. Rather, it is claimed that ventral visual areas become "tuned" to visual word recognition based on its innate function in visual processing and the experience of learning to read and engaging in this activity (Polk & Farah, 1998; Cohen et al., 2002).

While Farah's (2004) account could potentially explain the performance of our pure alexic patients (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), at least their impairment in letter and digit recognition and their reduced visual apprehension span, it seems unnecessary based on our data to suggest an area specialized for either one of these processes. Rather, we suggest that a more low level visual deficit affecting shape perception interferes with processing of single letters and digits in our patients, and that this may in itself be a sufficient explanation for their alexia. This low level deficit may perhaps be attributable to reduced sensitivity to important spatial frequencies (Fiset, Gosselin et al., 2006), or to impaired shape perception in foveal vision regardless of the spatial frequencies of the stimuli (Starrfelt, Habekost & Gerlach, 2008). In all the pure alexic patients reported here, this deficit was accompanied by a reduced visual apprehension span. Unlike Farah (1990), but in line with Duncan et al. (2003) we argue that this reduction should only have an effect on word reading if a deficit in the integration of letters into words is also present, as will be discussed below.

4.5. Processing of words and letters in dorsal and ventral visual streams

One interesting question raised by the current studies, is the relation between reduced visual apprehension span and impaired reading. A long standing hypothesis of pure alexia within cognitive neuropsychology is the simultanagnosia hypothesis suggested by Kinsbourne & Warrington (1962). Until the present, this hypothesis has kept surfacing, and as mentioned in the introduction, pure alexia may even be referred to as ventral simultanagnosia (Farah, 2004). In our patient studies (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), we found evidence of reduced visual apprehension span for both letters and digits in all patients. Yet, the relations

between reduced visual span and impaired reading is not straight forward. One reason for this is that patients with dorsal simultanagnosia, whose visual apprehension span can be smaller than in our alexic patients (commonly these patients can see only one item at a time), can still read single words. Thus, words seem to be one object to these patients, while in pure alexia / ventral simultanagnosia words seem to be reduced to their constituent parts (letters).

Although patients with dorsal simultanagnosia can read words, they do not necessarily read normally. Obviously, they have severe difficulties in reading text, as this demands shifting attention between objects, but even single word reading and single letter identification is commonly abnormally slow and error prone at least in patients with classical Balint's syndrome (Baylis et al., 1994; Hall, Humphreys & Cooper, 2001). The long reading latencies may relate to the severely reduced processing speed that seems to characterize dorsal simultanagnosia (Duncan et al., 2003), but their errors in reading can probably not be explained by this deficit. Patients with Balint's syndrome and dorsal simultanagnosia commonly show signs of *attentional alexia*, which is characterized by better identification of words than their constituent letters, and by migration errors when reading multiple words (*car* and *rattle* may be read *cattle*). While this is the normal pattern of performance in dorsal simultanagnosia, one report convincingly demonstrates that single word reading and single object identification can be normal, in spite of severe difficulties with identifying multiple objects and words (Coslett & Saffran, 1991). This patient did not have Balint's syndrome, but rather represented a quite pure case of dorsal simultanagnosia due to a right occiptio-temporo-parietal lesion, with only a small lesion in the left hemisphere that was clinically "silent". Importantly, Coslett & Saffran's (1991) patient, as well as other dorsal simultanagnosics (Baylis et al., 1994; Vinckier et al., 2006) show disproportional problems in reading nonwords. They also show severe reading problems when words are presented in an unfamiliar format, for instance when they are presented vertically or rotated (Vinckier et al., 2006), or in mIxEd CaSe (Hall et al., 2001). This led Vinckier et al (2006) to suggest that their patient's reading was impaired in conditions which would induce a word length effect in normals, that is, in instances where parallel letter analysis is not possible and attention must be directed to single letters. They further suggested that pure alexia is one instance where parallel letter processing breaks down even for words presented in canonical form.

While fluent reading / word recognition depends mainly on ventral left hemisphere structures, it seems that (right) parietal attentional functions may be important when reading unfamiliar words, nonwords and words presented in non-canonical form. As shown by Vinckier et

al. (2006) the pattern of performance by patients with dorsal lesions can inform us of the capabilities of the ventral visual stream, but what this study also makes clear is that normal reading very possibly is the result of both dorsal and ventral visual processing. This suggests that further investigation of the relation between dorsal and ventral processing in reading could be a fruitful venture in aiming to understand both alexic and normal reading. Interestingly, a similar line of reasoning can be found in the literature on developmental dyslexia (Pugh et al., 2000; 2001; Shaywitz, Mody & Shaywitz, 2006), where it has been hypothesized that dyslexic readers show deficits in both a dorsal (temporo-parietal) and a ventral (occiptio-temporal) pathway. In this literature, the ventral pathway is assumed to be a late developing word recognition system, while beginning reading (as well as nonword reading) is assumed to rely on processing mainly in the dorsal pathway (Pugh et al., 2000; 2001). It is the ventral system that is affected in pure alexia, and the residual reading abilities observed in our patients may perhaps rely on processing mainly in the dorsal visual stream. As attention to single letters seems to be a property of the dorsal pathway, which is intact in pure alexia, this may explain why patients resort to a letter-by-letter strategy to compensate for their loss of the fast and efficient processing through the ventral stream. The intactness of the ventral system may vary between patients, and this could potentially explain differing results with regards to top down effects in pure alexic reading, as well as the effect of visual short term memory capacity (VSTM-capacity) on reading. Also, depending on individual patients' residual letter identification abilities, their word reading latencies would be expected to differ. Note however, that in Fiset, Gosselin et al.'s (2006) study of normal subjects the observed word length effects varied considerably between subjects, indicating that individual factors not relating to symptom severity may also contribute to reading latency.

Following up on the word superiority experiment with NN (Starrfelt, Habekost & Gerlach, 2008), it would be interesting to further investigate the relationship between the observed reductions in processing capacity (speed and apprehension span) and word reading. Also, based on the studies on dorsal simultanagnosia (Hall et al, 2001; Duncan et al., 2003; Vinckier et al, 2006) it could be interesting to investigate the relation between attentional capacity and letter report from real words in non-canonical format in normal subjects. Based on Vinckier et al.'s (2006) reasoning, it would be expected that normal subjects' VSTM-capacity should influence their letter report from words presented in MiXeD cAsE or rotated, while they would be expected to exceed their capacity for reporting unrelated letters when words were presented in a canonical format.

In the five pure alexic patients presented in this dissertation (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), a significant reduction in visual apprehension span for both letters and digits was evident. Above it was argued that this deficit may contribute to the reading deficit because of an impairment affecting the integration of letters into words. While this integration deficit in itself may be sufficient to result in reading problems, reduced visual apprehension span in itself seems not to affect single word reading (Coslett & Saffran, 1991; Vinckier et al., 2006). However, accounting for how reduced visual apprehension span may affect reading does not explain why reduced apprehension span is associated with pure alexia. One possible reason is that this is related to the types of stimuli we employed in testing VSTM-capacity: letters and digits. In all the reported patients, processing efficiency even for single stimuli was impaired for these symbols, and thus these representations may be harder to encode. The results of patient JH (Starrfelt, Habekost & Leff, 2008) may speak against this hypothesis, as she was comparatively good at recognizing single digits, but who could still not encode more than two digits in the whole report experiment. Thus, there may well be a real relationship between the reduced visual apprehension span observed in our patients and pure alexia, and this may perhaps relate to Farah's (2004) suggestion of ventral visual areas being of particular importance for rapid processing of multiple visual forms. At present, the reason for this association or co-occurrence remains unresolved, but this deserves further investigation. One way to assess whether reduced visual apprehension span is an effect of degraded visual letter representations rather than a contributing factor in pure alexia, would be to investigate normal performance in whole report experiments with degraded stimuli. If degrading letters reduces *K,* then the reduced apprehension span observed in our patients may be an effect of degraded letter representations. Another way of assessing the generality of our estimates of VSTM-capacity in pure alexic patients would be to measure this with non-shape stimuli. Indeed, in designing the current studies we aimed at including a whole report task with colour stimuli. However, repeated pilot experiments revealed that the report of colour names was inherently difficult even for normals. Yet, this should be explored further, as it would provide a much needed tool for investigating visual attentional capacity in patients with shape perception deficits.

4.5. Cerebral specialization for reading?

Cohen et al. (2003; 2004) have suggested that the putative visual word form area is specialized for extracting abstract letter identities, and therefore it is of extreme importance in

reading. Important to a degree that when this area is damaged, this function is lost and patients have persistent reading problems. The studies reported here (Starrfelt & Gerlach, 2007; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008) supports the hypothesis that the VWFA is of special importance in reading, and that damage to this area and surrounding structures leads to mild pure alexia for which intact visual areas in the right hemisphere cannot compensate. Above it was argued that although object and number processing is also affected in pure alexia (at least in the patients reported here; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), their reading problem is the most disabling, and indeed seems to be the only problem of which the patients are aware. So why is reading so special? As has been pointed out, reading is a complex learned skill that places high demands on the visual system, perhaps higher demands than any other visuo-perceptual task: It demands rapid processing of multiple visual shapes; rapid discrimination between similar shapes; rapid integration of multiple shapes; rapid extraction of the optimal spatial frequencies; rapid planning and execution of eye movements; high foveal acuity; and this is only in the visual domain. Reading, of course, also demands rapid access to semantics and phonology. The word of the day seems to be *rapid*. Although it was argued above that reduced processing speed cannot in itself explain pure alexia (cf. Duncan et al., 2003), it must contribute, particularly when the reduced processing reflects reduced shape perception in central vision, rather than attentional factors. In the reported studies, we have aimed at comparing reading and letter identification to recognition of visual stimuli that may rely on the same visuo-perceptual processes as reading. However, even when comparing letters with digits, this comparison is not as close as one could have wished. Indeed, there seems to be no task quite like word reading. So perhaps parts of the visual system is specialized for reading in the sense that reading is the only function that demands a certain kind of visual processing.

In a recent review of the evidence for cerebral specialization for reading and face recognition, Kleinschmidt and Cohen (2006) suggest that there are two ways of conceptualising *cerebral specialization*. The first is concerned with whether *one brain region* (as opposed to many) underlies a defined function, for instance visual word recognition. The other demands that the region in question subserves only *one function*. Kleinschmidt and Cohen (2006) claim that the first type of specialization has been demonstrated for both faces (in the right fusiform gyrus) and written words (in the left fusiform gyrus). They state that it would "appear possible if not likely that a VWFA should also respond to other visual input types and maybe even to a similar extent" (p. 389), but still claim that the region of the VWFA is specialized in that only this brain region subserves

visual word recognition on an abstract level. When this region is lesioned, the ability for "fast computation of an ordered representation of abstract letter identities" is lost (Kleinschmidt & Cohen, 2006; p. 387) and the result is pure alexia. They further suggest that a lesion to this specialized area (and thus the function it subserves) provides "the most parsimonious account for (…) agnosic alexia" (p. 386). Their claim that the VWFA subserves a function of extreme importance in visual word recognition, and that other areas do not contribute to this function to a degree that they can subserve efficient reading seems reasonable based both on the literature in general and the studies presented here (Starrfelt & Gerlach, 2007; Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008). The suggestion of a reproducible localization of the VWFA across individuals, suggested by Cohen and Dehaene (2004) to be a form of specialization, is also supported; in the PET study (Starrfelt & Gerlach, 2007) we did find that the VWFA was activated more by words than pictures in some tasks. In addition, all the reported pure alexic patients have lesions affecting the VWFA (Starrfelt, Habekost & Gerlach, 2008; Starrfelt, Habekost & Leff, 2008), and this may well be the main cause of their alexia. Attempts to ameliorate pure alexic symptoms through training have had limited success, and this does speak for a degree of specialization in the VWFA and surrounding structures. It seems that even with years of practise *after* acquiring pure alexia, these patients do not reach normal levels of reading speed and fluency. However, the most parsimonious explanation for pure alexia may still be found in a general visual process, rather than in a system or area specialized for extracting abstract letter identities, and it will be important in future research to further specify the processes involved in visual word recognition.

5. Concluding comments

The debate of the visual word form area has sparked an increased interest in understanding the processes responsible for recognition of written words and how these can break down as a result of brain injury, and this has generated a large literature concerning pure alexia and visual word recognition. This dissertation has aimed to add to this literature, and will hopefully contribute to the further understanding of how written words are recognized, how this process can be damaged, and perhaps in the end how visual deficits affecting word recognition can be ameliorated or more effectively compensated for. With the aid of sensitive measurements and meaningful stimulus comparisons, data have been collected that shed light on visual processing in pure alexia, and on normal visual processing of words and objects within the putative visual word form area. It is a

humble contribution, in that reading is not only visual recognition of letters and words, but a process that demands many other cognitive functions such as central language processes, semantics, phonology and motor action, all of which seem to be intact in pure alexia. As demonstrated in this dissertation, disentangling the processes involved in recognizing written words is not an easy matter. Moreover, it seems that although visual word recognition and other visual processes are connected and interact, there is something special about processing of written words in comparison with other visual stimuli. Based on the current studies, it seems that in the ventral visual stream, and perhaps in particular in the left fusiform gyrus, the first bottleneck in the reading process is to be found.

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