



## Research Report

# Visual processing of words in a patient with visual form agnosia: A behavioural and fMRI study



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## ABSTRACT

Patient D.F. has a profound and enduring visual form agnosia due to a carbon monoxide poisoning episode suffered in 1988. Her inability to distinguish simple geometric shapes or single alphanumeric characters can be attributed to a bilateral loss of cortical area LO, a loss that has been well established through structural and functional fMRI. Yet despite this severe perceptual deficit, D.F. is able to “guess” remarkably well the identity of whole words. This paradoxical finding, which we were able to replicate more than 20 years following her initial testing, raises the question as to whether D.F. has retained specialized brain circuitry for word recognition that is able to function to some degree without the benefit of inputs from area LO. We used fMRI to investigate this, and found regions in the left fusiform gyrus, left inferior frontal gyrus, and left middle temporal cortex that responded selectively to words. A group of healthy control subjects showed similar activations. The left fusiform activations appear to coincide with the area commonly named the visual word form area (VWFA) in studies of healthy individuals, and appear to be quite separate from the fusiform face area (FFA). We hypothesize that there is a route to this area that lies outside area LO, and which remains relatively unscathed in D.F.

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## 1. Introduction

Patient D.F. has been one of the most intensively studied cases of visual agnosia in the literature over the past 25 years (Goodale, Milner, Jakobson, & Carey, 1991; Milner, 1998; Milner & Goodale, 2006; Milner et al., 1991). The reasons for this interest have been multiple. First, D.F. is remarkably well preserved, despite her severe carbon monoxide poisoning incident in 1988: she has no problems with motor coordination, and has no serious impairments in intellect, memory, visual perception of

colour or texture, or in non-visual perception. Second, despite her profound visual form agnosia, D.F. has well-preserved visually guided movements, including reaching, grasping, saccadic eye movements, locomotion, and obstacle avoidance. There are limits on the visual complexity of the stimuli that can guide her grasping behaviour (Dijkerman, Milner, & Carey, 1998; Goodale et al., 1994; McIntosh, Dijkerman, Mon-Williams, & Milner, 2004), but D.F.'s dissociation between preserved visuo-motor control and impaired shape perception is fully consistent with the Two Visual Streams model of Milner and Goodale (2006), and indeed helped inspire the model in the first place.

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According to that model, the occipito-temporal “ventral stream” of visual areas underlies our perception and recognition of the world, whereas the occipito-parietal “dorsal stream” provides the real-time visual control for our movements. In line with the model, D.F. subsequently turned out to have complete bilateral destruction of the lateral occipital area (LO) in the ventral stream, an area that functional MRI (fMRI) research has linked closely with shape perception (James, Culham, Humphrey, Milner, & Goodale, 2003). Furthermore, despite an absence of any net fMRI responses to visual shape in her ventral stream, D.F. was found still to show responses in her dorsal stream during object grasping in areas associated with visual control of such movements [specifically the human anterior parietal area (hAIP)].

The original description of D.F. (Milner et al., 1991) set out in detail her problems in visual perception, but also contains a puzzling discrepancy. Despite her profound difficulty in recognizing and discriminating the simplest of visual shapes, and indeed her equally severe difficulty in recognizing and discriminating single alphanumeric symbols, she nevertheless performs remarkably well when asked to identify whole words. D.F. often responds incorrectly, particularly with less common words, yet her errors are frequently visual in nature, for example money–honey, ring–right, and environment–improvement. Subjectively, D.F. generally says that she is guessing, but her behavioural success is remarkable, typically being better with longer than with shorter (2–3 letter) words. We found these data surprising in 1991, but in hindsight, we now hypothesize that perhaps D.F. retained a preserved “visual word form area” (VWFA) in the left mid-fusiform gyrus of her left hemisphere, a region which anatomical MRI scans suggested remains largely intact. The present study was designed to test this hypothesis, whose plausibility trades on the fact that fMRI activations can be recorded from her “fusiform face area” (FFA) (Steeves et al., 2006) and her “parahippocampal place area” (Steeves et al., 2004) despite her poor performance on tests of face discrimination or of scene discrimination, respectively.

The history of research on the so-called VWFA has been a chequered one. The term was first coined by Abdullaev and Posner (1998) in relation to an event-related potential negativity (ERP) negativity at around 200 msec post-stimulus in the left occipital region. However, activation in this region had been previously recorded in responses to visual words during PET studies many years earlier by Petersen, Fox, Posner, Mintun, and Raichle (1988) and Petersen, Fox, Snyder and Raichle (1990), who had already argued that the area was concerned with identifying the visual form of printed words. Even earlier, Warrington and Shallice (1980) had postulated the existence of an early system for identifying word form on the basis of their research on reading in patients with “pure alexia”, whose apparent loss of the ability to perceive whole words required them to depend on a letter-by-letter strategy. Subsequently, Puce, Allison, Asgari, Gore, and McCarthy (1996) reported activation in the left occipito-temporal area associated with letter strings. Puce and colleagues' findings were replicated by Cohen et al. (2000), who also used fMRI to locate a region responsive to words in the left fusiform gyrus. Since then, regular doubts as to the status of the VWFA have been expressed, starting with the publication of Price and Devlin's

critique in (2003), and there is no question that studies using fMRI have yielded varying results. Some authors have accordingly adopted a less contentious label for the area (e.g., “posterior occipito-temporal sulcus (pOTS)”; Ben-Shachar, Dougherty, Deutsch, & Wandell, 2007). Nevertheless the current consensus agrees that the left mid-fusiform gyrus is consistently activated by the presentation of words or pseudo-word letter strings (Cohen & Dehaene, 2004; Cohen et al., 2002; Dehaene & Cohen, 2011; Nestor, Behrmann, & Plaut, 2013), and that patients with pure alexia almost invariably have lesions affecting the left fusiform gyrus or its connections (Cohen et al., 2003; Leff et al., 2001). Therefore in this report we will refer to this area as the “VWFA”, which remains the label that is most commonly used in the literature.

Our hypothesis is that D.F.'s partial ability to identify whole words relies on a largely intact VWFA, but that this spared area is subject to severely depleted visual inputs. We assume that the major visual route to the VWFA in the normal brain would provide information from shape processing mechanisms within area LO, an area that is no longer functional in D.F. This would explain her inability to discriminate single letters. We assume, however, that there must exist a parallel pathway from earlier visual areas to the VWFA, bypassing the lateral occipital complex, and that this may remain largely intact in D.F. The hypothesized parallel pathway to the VWFA could well pass through the inferior longitudinal fasciculus, which diffusion tensor imaging (DTI) analysis has shown to provide the main afferent route to the VWFA (Epelbaum et al., 2008). Of course the functioning of the VWFA would be expected to suffer severely as a result of losing its normal inputs from area LO, and in particular this loss may deprive the VWFA of any residual ability to contribute to the normal phenomenology associated with word recognition. In other words, such impoverished visual inputs to VWFA could explain why it is that D.F. experiences her efforts to identify words as merely “guessing”.

Previous investigations (Cohen et al., 2000, 2002; Hasson, Levy, Behrmann, Hendler, & Malach, 2002) have indicated that the VWFA lies in close proximity to the left FFA in healthy subjects. Structural and fMRI data from recent studies of D.F. (Bridge et al., 2013; Cavina-Pratesi, Kentridge, Heywood, & Milner, 2010b) indicate that her fusiform gyrus as a whole is structurally intact at a gross level. In particular the tissue lying around the left lateral occipito-temporal sulcus seems to be spared. Thus it is plausible to suppose that the VWFA might indeed be structurally intact in D.F. To test this hypothesis we tested D.F. using an fMRI localizer in which we contrasted the activations elicited by English words against those elicited by strings of digits. We also presented strings of Hebrew characters, random letters and line drawings for comparison (Baker et al., 2007).

Following this localizer study we ran a second experiment in which we attempted to clarify the response characteristics of the area we had tentatively identified as the VWFA in D.F. Dehaene and Cohen (2011) have argued that neurons in VWFA are tuned to fragments of written words. According to his “local combination detector model” (Dehaene, Cohen, Sigman, & Vinckier, 2005), VWFA neurons comprise a hierarchy of receptive fields tuned successively to letters, bigrams (letter pairs), morphemes and small words. fMRI studies (Binder,

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