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Why people see things that are not there: A novel Perception and Attention Deficit model for recurrent complex visual hallucinations

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Abstract: As many as two million people in the United Kingdom repeatedly see people, animals, and objects that have no objective reality. Hallucinations on the border of sleep, dementing illnesses, delirium, eye disease, and schizophrenia account for 90% of these. The remainder have rarer disorders. We review existing models of recurrent complex visual hallucinations (RCVH) in the awake person, including cortical irritation, cortical hyperexcitability and cortical release, top-down activation, misperception, dream intrusion, and interactive models. We provide evidence that these can neither fully account for the phenomenology of RCVH, nor for variations in the frequency of RCVH in different disorders. We propose a novel Perception and Attention Deficit (PAD) model for RCVH. A combination of impaired attentional binding and poor sensory activation of a correct proto-object, in conjunction with a relatively intact scene representation, bias perception to allow the intrusion of a hallucinatory proto-object into a scene perception. Incorporation of this image into a context-specific hallucinatory scene representation accounts for repetitive hallucinations. We suggest that these impairments are underpinned by disturbances in a lateral frontal cortex–ventral visual stream system. We show how the frequency of RCVH in different diseases is related to the coexistence of attentional and visual perceptual impairments; how attentional and perceptual processes can account for their phenomenology; and that diseases and other states with high rates of RCVH have cholinergic dysfunction in both frontal cortex and the ventral visual stream. Several tests of the model are indicated, together with a number of treatment options that it generates.

Keywords: Blindness; Charles Bonnet; cholinergic; cortical release; delirium; dementia; dream intrusion; hallucination; Perception and Attention Deficit (PAD) model; schizophrenia.

1. Introduction

Is this a dagger which I see before me,
The handle toward my hand? Come, let me clutch thee:
I have thee not, and yet I see thee still.
Art thou not, fatal vision, sensible
To feeling as to sight? or art thou but
A dagger of the mind, a false creation,
Proceeding from the heat-oppressed brain?
I see thee yet, in form as palpable
As this which now I draw.
—Macbeth, Act II Scene 1

"I see people who are not there. I see people in the street with clipboards, sometimes it's the same person turning up, little fat chap, looks like Mickey Rooney."
—M.D. (A person with visual hallucinations associated with schizophrenia)

More than one million adults in Britain, while awake, repeatedly see people, animals, or objects that appear real but are not visible to others. Perhaps half as many again have similar experiences on the borders of sleep. Few, though, express their experiences quite so eloquently, or indeed publicly, as Shakespeare's Macbeth. For many, hallucinations are emotionally neutral or even comforting experiences (e.g., Diederich et al. 2000; Grimby 1993; 1998; Paulson 1997; Risser & Powell 1993; Tien 1991). For others, they are distressing and disabling symptoms of major illnesses (e.g., Goetz 1999; O'Reilly & Chamberlaine 1996). A general functional model may aid our understanding of these phenomena and ultimately lead to better help for these latter groups (e.g., Collerton & Dudley 2004).

Single experiences of visual hallucinations are so com-

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mon as to be considered normal. McKellar (1957) reports single hypnagogic hallucinations in 63% of students, and Ohayon (2000) reports that "almost everybody" has experienced at least one hypnopompic or hypnagogic hallucination. In this target article, we will be focusing on those people who have recurrent and potentially pathological hallucinations. Recurrent complex visual hallucinations (RCVH) are uncommon in non-pathological populations, with estimates in the 0.3% range for one or more per month (Ohayon 2000). Increasing frequency is associated with greater pathology (Ohayon 2000), as is longer persistence. Holroyd and Rabins (1996) and Gauntlett-Gilbert and Kuipers (2003) describe how they may persist in eye disease and schizophrenia over many years.

We will also primarily deal with complex, or formed, hallucinations of people, animals, and objects. Classically, these are differentiated from simple hallucinations of dots, lines, flashes, and amorphous shapes, as well as from panoramic hallucinations of landscapes (Cutting 1997, p. 84). Since these latter may result from different mechanisms (see, e.g., Cole 1999; Manford & Andermann 1998; and sect. 3.1 here), we will address them only in passing.

Recognition of hallucinations as potentially pathological biological phenomena dates from at least the medieval period. There are ninth-century Persian descriptions of *shaqhiqheh*, a headache associated with visual hallucinations (Gorji & Ghadiri 2002). In Europe, Charles Bonnet described them in the eponymous eye disease in 1769 (Schultz & Melzack 1991).[1] In recent times, several distinct models of visual hallucinations have been developed from the perspectives provided by mechanistic understandings of different disorders such as eye disease (e.g., ffytche & Howard 1999; Menon et al. 2003; Santhouse et al. 2000; Schultz & Melzack 1991), epilepsy (e.g., Kolmel 1993; Levine & Finklestein 1982; Rabins et al. 1991), sleep disorders (e.g., Arnulf et al. 2000; Manni & Mazzarello 2001; Manni et al. 2002; Nomura et al. 2003; Risser & Powell 1993), psychosis (e.g., Flynn 1962; Horowitz 1975; Slade & Bentall 1988), and Parkinson's disease (Barnes et al. 2003). These have been largely successful in accounting for hallucinations in specific disorders but struggle to generalise outside of the areas where they were developed.

We have generated a new Perception and Attention Deficit (PAD) model, initially to account for hallucinations in a recently recognised disorder, dementia with Lewy bodies (McKeith et al. 2003), in which RCVH are exceptionally common. We will show how this model cannot only be successfully generalised to RCVH in other neurodegenerative disorders, but also how it has the potential to account for consistencies in the experience of RCVH in non-degenerative disorders and for non-pathological RCVH occurring during the transition between sleep and waking.

In doing this, we accept that active, ceaseless, complex, dynamic interactions between the visual systems and other brain areas lead to subjective perception. Many dysfunctions, either relative or absolute, in one or more areas might lead to consequent effects in others that are experienced as different types of hallucinations. Hence, perhaps, the great variability in type, content, frequency, and associated phenomena of RCVH (Brasic 1998; Kolmel 1993; Schultz et al. 1996). Like others (e.g., Behrendt & Young 2004; Manford & Andermann 1998), we do not see that it is the role of a general model to account for all this limitless variety. If we believe that visual dreams, hallucinations, volitional images, and perception reflect the activity of the same system operating under different constraints, then the role of a general model (if such can be found) is to identify the constraints that produce hallucinations. Thus, it should explain consistencies between different experiences. To this end, our strategy has been to draw out the similarities between different experiences in different disorders, averaging data wherever possible. Though this runs the risk of creating apparent commonalities where none truly exist, and obscuring as much as it illuminates, we feel that this is justified in an attempt to bring greater order to what has been a fragmented field of enquiry.

2. Defining and assessing recurrent complex visual hallucinations

Investigating normal visual imagery is challenging (Reisberg et al. 2003; Schwitzgebel 2002). Investigating halluci-

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natory visual imagery is perhaps even more so (Taylor et al. 1986), not least because there is no consensus definition or classification (Cutting 1997). Hallucinations are generally defined as perceptions without stimuli (Asaad & Shapiro 1986; Brasic 1998; Kolmel 1993). In contrast, illusions or misperceptions are incorrect perceptions of stimuli (Brasic 1998; Kolmel 1993). Horowitz (1975) takes an intermediate position and defines a hallucination as an "image experience in which there is a discrepancy between subjective experience and actual reality." As definitions, these do not formally distinguish between self-generated imagery, dreams, and hallucinations. They are also at odds with constructive models of subjective perception (e.g., Behrendt & Young 2004; Friston 2002a; 2002b; Rees 2001). These see a loose relationship between stimuli and perception, with many aspects of normal perception occurring in the absence of current sensory input. Indeed, an argument can be made, albeit not entirely convincingly (Clark 2002), for normal perception being mostly hallucinatory. For the purposes of this article, we will therefore sidestep these definitional problems and operationally define recurrent complex visual hallucinations (RCVH) as repetitive involuntary images of people, animals, or objects that are experienced as real during the waking state but for which there is no objective reality.

Between 75% and 90% of hallucinators do not spontaneously reveal their experiences (Nesher et al. 2001; Scott et al. 2001; Teunisse et al. 1996), with a good proportion not identified during routine assessments (Bracha et al. 1989). When hallucinations are identified, there is a lack of validated tools for the subjective or objective assessment and classification of hallucinatory experiences.

Differentiating between hallucinations and illusions or misperceptions is also challenging. Thus, there are instances where misinterpretations seem very unlikely, for example, hallucinating a person sitting on a chair; and there are those where misperception appears likely, for instance, mistaking one person for another. However, there can be significant difficulties in a grey zone of intermediate experiences in which patterns on walls or cushions, for example, metamorphose into faces. Additionally, many patient groups with high rates of apparent hallucinations, such as psychosis or dementing illnesses, also have high rates of other visual or communication problems (see sect. 3.1; Ballard et al. 1999; O'Brien et al. 2000). For example, Horowitz (1964) describes how patients with schizophrenia can attach meaning to simple visual hallucinations and hence report them as if they were complex; as instances, reporting lines as "vicious snakes" or dots as "two armies struggling over my soul." Compounding these problems are the great variations between studies in the methods used to identify, assess, classify, and report hallucinations.

Despite these caveats, we believe that there is enough epidemiological, phenomenological, pathological, psychological, and imaging evidence to allow us to develop and test general models of RCVH. We will now review that evidence.

3. People who see things

Many, many diseases, brain lesions, pharmacological agents, and psychological states are reportedly associated with RCVH (for qualitative reviews, see Anderson & Rizzo 1994; Asaad & Shapiro 1986; Brasic 1998; Kolmel 1993; Manford & Andermann 1998).

3.1. Associated states and diseases

The prevalence of hallucinations shows distinct variation between conditions (Fig. 1). Some of this will reflect random or systematic biases. For example, reported rates of RCVH in eye disease range from below 1% to above 10% depending partially on selection and exclusion criteria (Shiraishi et al. 2004); and some disorders with particularly high rates (i.e., dementia with Lewy bodies, see McKeith et al. 2003; and narcolepsy, see Aldrich 1996) have visual hallucinations as one possible diagnostic criteria. There is a need for direct, within-study comparisons between different disorders. Even so, it is striking that acquired eye disease, occipital stroke, and sensory deprivation, all causes of restricted visual input, have similar low rates of RCVH (3–18%). Disorders with more distributed dysfunction, for example, those associated with disturbed consciousness (e.g., narcolepsy and delirium), some dementing illnesses (dementia with Lewy bodies, Parkinson's disease with dementia, and vascular dementia), and schizophrenia have high rates (30–59%). Table 1 shows that, where data exist, frequencies are in some cases reversed for simple hallucinations. Thus, simple hallucinations are relatively frequent in sensory deprivation and eye disease, but infrequent in dementia, delirium, and Parkinson's disease. This double dissociation between simple and complex hallucinations suggests two things to us. First, that each type of hallucination has a single primary cause, and second, that these causes are separable within the visual system.

These estimates of frequency within categories can be combined with estimates of the frequencies of these categories in, for example, the UK adult population to give an admittedly crude indication of associations with RCVH in the general population (Fig. 2). Normal hypnopompic (on waking) and, especially, hypnagogic (on falling asleep) hallucinations are, overall, the most frequent types. Broadly speaking, four groups of disorders – delirium, age-related dementia, schizophrenia, and acquired eye disease – stand out as being most frequently associated with RCVH. In contrast, some disorders that have been used to support general models (thalamic and pedunculopontine hallucinosis; see Noda et al. 1993; Risser & Powell 1993); stimulation of the subthalamic nucleus (Diederich et al. 2000); and fatal familial insomnia (Gallassi et al. 1996; Tabernero et al. 2000) are much rarer.

A number of risk factors for RCVH within specific disorders have been reported (Table 2), though there have been no cross-category comparisons and there are some contradictions (e.g., whether depression in Parkinson's disease is or is not associated with hallucinations). Increasing intellectual impairment is a consistent risk factor as is poor vision, though significantly, hallucinations cease in eye disease when all vision is lost (Menon et al. 2003). Impaired alertness or sleep abnormalities are also a recurring theme, even aside from delirium and narcolepsy. This suggests either that these categories overlap, or as others have also suggested (e.g., Cole 1992; Menon et al. 2003; Pappert et al. 1999), there may be a consistent set of features that predispose an individual patient to developing RCVH – namely, intellectual impairment, poor vision, and disturbed alertness.

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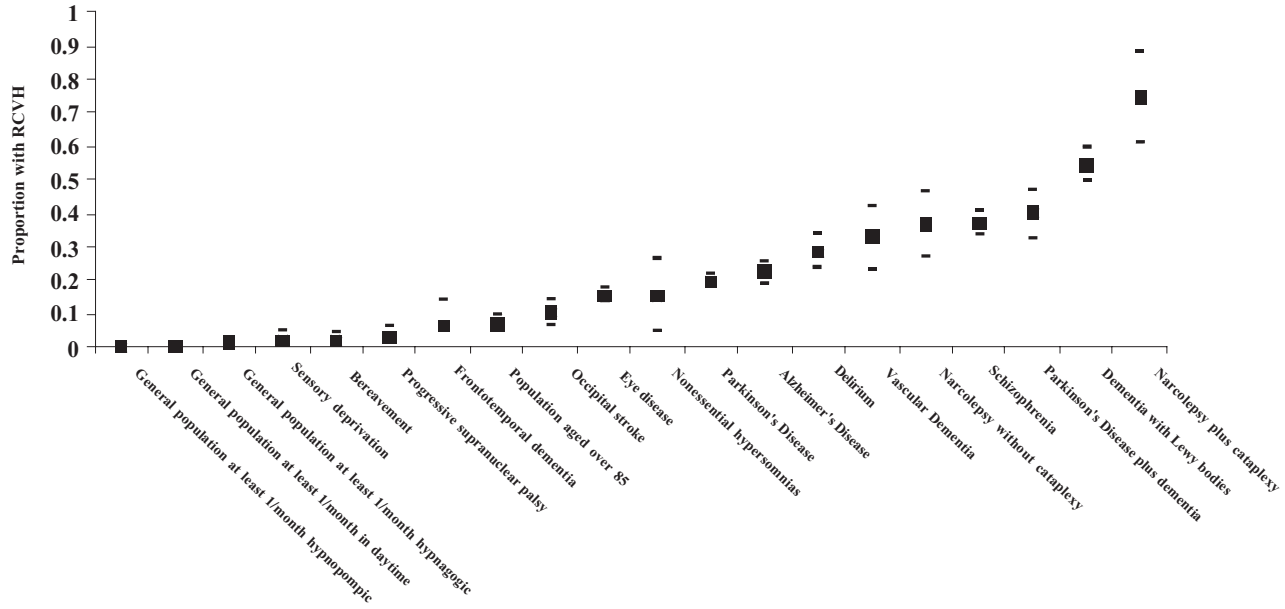

Figure 1. Reported frequencies of RCVH within different normal and pathological states. Values are averaged proportions (weighted by sample size) plus or minus 95% CI. Disparate methodologies and subject groups will account for some of the variation between groups. Both random and systematic biases cannot be excluded at present. Sources: dementia with Lewy bodies (Aarsland et al. 2001a; Ballard et al. 1995b; 1999, including six reviewed studies; 2001); Parkinson's disease (Aarsland et al. 2001a; 2001b; Barnes & David 2001; Cummings 1991; Fenelon et al. 2000; Goetz 1999; Holroyd et al. 2001; Sanchez-Ramos et al. 1996); Parkinson's disease plus dementia (Aarsland et al. 2001b; Neimark et al. 1996); progressive supranuclear palsy (Aarsland et al. 2001b); eye disease (Brown & Murphy 1992; Holroyd et al. 1992; Kolmel 1993; Lepore 1990; Scott et al. 2001; Soros et al. 2003); Alzheimer's disease (Ballard et al. 1995b; 1999; 2001; Bathgate et al. 2001; Cummings et al. 1987; Holroyd & Sheldon-Keller 1995); vascular dementia (Ballard et al. 1995b; Bathgate et al. 2001; Cummings et al. 1987); delirium (Cutting 1997; Webster & Holroyd 2000); sensory deprivation (McKellar 1957; Schulman et al. 1967); general population (Lindal et al. 1994; Ohayon et al. 1996; 2000); occipital stroke (Anderson & Rizzo 1994; Kolmel 1993; Vaphiades et al. 1996); people over 85 (Ostling & Skoog 2002); schizophrenia, including paraphrenia (Bracha et al. 1989; Cutting 1997; Howard et al. 1994; Ndetei & Singhe 1983; Zarroug 1975); narcolepsy and essential hypersomnias (Aldrich 1996); frontotemporal dementia (Bathgate et al. 2001); bereavement (Grimby 1993).

3.2. Pharmacologically induced hallucinations

Evidence that the phenomenology of RCVH is more consistent with hallucinations induced by anticholinergic drugs than by drugs acting on 5-HT, noradrenergic, glutamate, or GABA systems has been reviewed previously (Perry 2002; Perry & Perry 1995), although one notable difference is that drug-induced hallucinations occur with both eyes open and with eyes closed.

Antimuscarinic drugs used in ophthalmology, anaesthesia, heart disease, or motion sickness, and also used ritualistically or recreationally, most frequently induce hallucinations of people and animals in normal individuals (reviewed Perry & Perry 1995; see also Balikova 2002; Cheng et al. 2002; Gopel et al. 2002; Han et al. 2001; Tune 2000; Tune & Egeli 1999; Winawer 2001), especially in the young and elderly (in whom cortical cholinergic activity is lower than in adults; Perry et al. 1992). Nicotinic, as well as muscarinic, receptors may be involved since toxic quantities of tobacco can induce hallucinations (Thomas 2002).

In Parkinson's disease, antimuscarinic agents such as atropine can induce hallucinations (Cummings 1991; Hyson et al. 2002). There is also a limited amount of evidence that patients with dementia with Lewy bodies are vulnerable to potentially hallucinogenic effects of neuroleptic medication with anticholinergic side effects (Scheepmaker et al. 2003). There is consistent evidence that antimuscarinic drugs induce delirium with hallucinations, especially in the elderly (Han et al. 2001; Tune 2000). Endogenous antimuscarinic activity in plasma has been reported in elderly medical patients with acute illness – a population at risk for delirium. This activity, which was not identified chemically, was detected using a broad spectrum anti-muscarinic receptor assay (Flacker & Wei 2001; Mussi et al. 1999). Delirium has also been reported as a result of nicotine withdrawal in heavy smokers (Mayer et al. 2001). Recent reports that the anticholinergic side effects of neuroleptic medication contribute to the cognitive deficits of schizophrenia (Minzenberg et al. 2004) raise the possibility that RCVH in this disorder are at least partially iatrogenic.

The case for a dysfunctional cholinergic basis for RCVH is strengthened by their symptomatic reduction in dementia with Lewy bodies, Alzheimer's disease, Parkinson's disease, and delirium by drugs which increase synaptic acetylcholine (physostigmine, donepezil, rivastigmine, galantamine; see McKeith et al. 2000; Bullock & Cameron 2002; Fabbrini et al. 2002; Maclean et al. 2001; Reading et al. 2001; Rosler et al. 1998; Zesiewicz et al. 2001).

In contrast to anticholinergic drugs, those (such as LSD) that target 5HT2 receptors induce phenomenologically different visual hallucinations that involve distorted images and synesthesia (blending of sensory modulators; Abraham et al. 1996; Perry 2002), though mianserin and ondansetron (5HT2 receptor antagonists) are reported to reduce visual hallucinations in Parkinson's disease (Ikeguchi & Kuroda 1995; Zolden et al. 1995). GABA may also be implicated

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Table 1. *Content of recurrent complex visual hallucinations*

	Complex hallucinations						Simple hallucinations	Panoramic hallucinations
PATIENT GROUP	Familiar people	Unfamiliar adults	Children	Animals	Inanimate objects	Multiple images		
Dementia with Lewy bodies	66[3]		8[3]	35[3]	11[3]		8[3]	
Parkinson's disease	15 (69 of all hallucinations unfamiliar)[1]			7[1], 10[2], 7[4], 8 (PDD)[3]	8[1], 4[4], 6[2], 3 (PDD)[3]		25[4], 4[2], 3 (PDD)[3]	
	11[4], 1[2]	13[4], 11[2]	3[2], 6 (PDD)[3]					
	40 (PDD)[3]							
Dementia (mixed diagnoses)	7[5]	20[5]	17[5], 5[8]	13[5], 6[8]	9[5]		0[5]	
	25[8]							
Eye disease		2[6], 2 (figures)[10], 8 (distorted faces)[10]	6[10], 1[16]	5[12], 3[13], 4[15], 1[16]	6[10], 9[12], 1[15], 1[13]	4[13], 13[24], 7[16], 12[12]	6[22], 2[16], 2[17], 18–20[10], 51[12], 17[19]	3[12],3[16], 6[22]
	1 (1 faces)[16]							
	21 (7 faces and body parts)[12], 11[13]							
	6[19], 13[22]							
Unselected population sample	2[11]	6[11]		1[11]			1[11]	
Delirium	27[9]			17[9]	11[9]		1[9]	
Schizophrenia (including paraphrenia)	20[9], 23[18], 58[21]			6[9], 3[18], 3[21], 6[11]	6[9], 3[18]	60[18]	64[14], 6[9], 31[11], 8[20], 50[14], 7[18]	
	18[11]	25[11]						
	64[14], 33[20]							
Stroke in visual pathways	22[17]						25[17]	
Alcohol abuse	79 (predominantly people)[14]						61[14]	
Sensory deprivation	6[23]						42[23]	

Figures are reported percentages of people who have hallucinations of each type out of all people who have that disorder. Because people may experience more than one type of hallucination, percentages may total more than 100%. Some sources (6, 7, 10, 15) reported rates only within those who hallucinated. In these cases, overall rates of 15% of people with eye disease having complex hallucinations and 25% with simple hallucinations were derived from other studies and used to calculate comparable figures.

Sources: (1) Holroyd et al. (2001); (2) Barnes & David (2001); (3) Aarsland et al. (2001a); (4) Fenelon et al. (2000); (5) Murgatroyd & Prettyman (2001); (6) ffytche & Howard (1999); (7) Brown & Murphy (1992); (8) Ballard et al. (2001); (9) Cutting (1997); (10) Santhouse et al. (2000); (11) Lindal et al. (1994); (12) Lepore (1990); (13) Nesher et al. (2001); (14) Deiker & Chambers (1978); (15) Pliskin et al. (1996); (16) Teunisse et al. (1996); (17) Vaphiades et al. (1996); (18) Gauntlett-Gilbert & Kuipers (2003); (19) Soros et al. (2003); (20) Howard et al. (1994); (21) Zarroug (1975); (22) Scott et al. (2001); (23) Schulman et al. (1967); (24) Needham & Taylor (2000).

PDD, Parkinson's disease with dementia.

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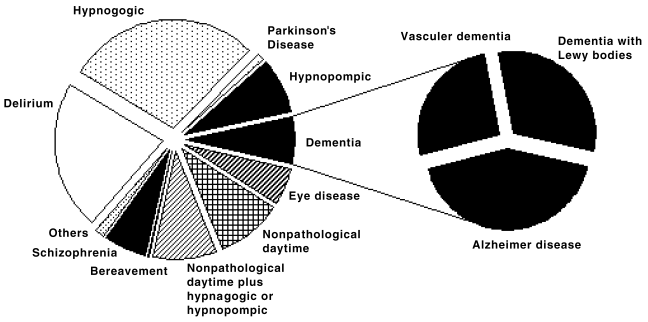

Figure 2. Estimated relative associations of RCVH in the adult population derived from reported frequencies within categories and prevalences of those categories. Data were calculated by multiplying the weighted average frequency of RCVH within each category (from Fig. 1) by estimates of prevalence of that category within the UK adult population (45.8 million; www.statistics.gov.uk). Estimates for the prevalence of specific categories are: dementia with Lewy bodies (150,000), vascular dementia (112,500), and Alzheimer's disease (412,500) (calculated from rates in Stevens et al. 2002); schizophrenia (1% of adult population; www.nelh.nhs.uk); delirium (22% [www.psych.org] of 9.6 million hospital inpatients, prorated from England figures; www.doh.gov.uk); repeated non-pathological day time (0.57% of population), hypnagogic (1.7%) and hypnopompic (0.5%) (Ohayon 2000; Ohayon et al. 1996); eye disease (1 million; www.rnib.org.uk); Parkinson's disease (120,000; parkinsons.org.uk); and bereavement (1% of the adult population; www.statistics.gov.uk). Others include rare disorders (under 0.5% of the population), or unsystematic series, or single case reports, for example, epilepsy, stroke, narcolepsy, pedunculopontine hallucinosis, fatal familial insomnia, and progressive supranuclear palsy. Because of variations between studies and disorders in definitions of RCVH, the data indicate approximate associations with RCVH rather than exact ratios. Estimating an average overlap among categories of a third gives a crude estimate of around 2 million adults with RCVH.

based on limited evidence of zolpidem induced visual hallucinations (Markowitz & Brewerton 1996), baclofen withdrawal (Harrison & Wood 1985), and delirium tremens (Brailowsky & Garcia 1999).

Agents such as mescaline that affect catecholaminergic systems, promoting the release of dopamine, are said to result in multi-coloured images of fantasy. The dopaminergic system is frequently implicated in disease-related visual hallucinations, especially in Parkinson's disease, on the basis of symptomatic treatment with neuroleptics such as clozapine (Devanand & Levy 1995; Molho & Factor 2001), which commonly target the D2 receptor subtype (although other pharmacological actions may be implicated), and on the basis of the induction of hallucinations by levodopa (L-dopa) (Cannas et al. 2001; Goetz et al. 2001a; 2001b; Holroyd et al. 2001). However, in Parkinson's disease, evidence that L-dopa is the principal contributing factor to hallucinations is not consistent, since increasing L-dopa medication does not increase hallucination prevalence (Goetz et al. 1997; 1998a). Among neuroleptics, olanzapine is reported to be superior in reducing hallucinations in Parkinson's disease, compared to haloperidol or risperidone (Edell & Tunis 2001) which could be related to the promotion of acetylcholine release associated with this type of drug (Ichikawa et al. 2002). In contrast to degenerative dementia, neuroleptics are not consistently effective in treating RCVH in the Charles Bonnet syndrome (Batra et al. 1997), and it remains to be determined if cholinergic agents are effective.

In conclusion, pharmacological data so far available indicate a primary role for cholinergic and secondary role for dopaminergic dysfunction in the aetiology of RCVH. Cholinergic hypoactivity alone, or dopaminergic hyperactivity if (and only if) cholinergic hypoactivity is already present, as underlying mechanisms are both consistent with the psychopharmacological evidence (above) and pathological data (sect. 7.6.2.2). In relation to the potential dual transmitter role, combined cholinergic and neuroleptic treatment is reported to be effective in reducing hallucinations in Alzheimer's disease (Bergman et al. 2003).

4. The character of recurrent complex visual hallucinations

4.1. Phenomenology

The content of RCVH is summarised in Table 1; and their phenomenology, in Table 3. As with estimates of the frequency of RCVH, there are contradictions and gaps in the data. Given the differences in methodology between studies and in the reporting abilities of different groups and the absence of direct comparisons of RCVH across disorders, it is unclear exactly how phenomenologically similar RCVH are in, say, eye disease, schizophrenia, and dementia. However, like previous reviewers (e.g., Behrendt & Young 2004; Brasic 1998; Cutting 1997; Horowitz 1975; Horowitz et al. 1968; Kolmel 1993; Manford & Andermann 1998; Siegel & Jarvik 1975), we consider that, in contrast to the variations in frequency of RCVH across disorders, the phenomenology of RCVH is more consistent. Together with the double dissociation between simple and complex hallucinations, this suggests to us that the wide range of factors associated with RCVH converge on a common target system.

4.1.1. Content. As we noted earlier in section 2, a distinction needs to be drawn between what is actually seen, which may be prosaic, and what is reported, which may be anything but. Many single case reports have emphasised the bizarre or incongruous nature of hallucinations (e.g., Needham & Taylor 2000; Silbersweig et al. 1995), but in our experience, within dementing illnesses (Mosimann et al., in press) and in systematic surveys (Cole 1992; Pliskin et al. 1996; Teunisse et al. 1996; Zarroug 1975), these are less common than rather commonplace images – a man sitting on a chair or a dog in the corner of the room, for example.

Hallucinations of people tend to be more common than are those of animals. Images of objects such as tables or cars are the least frequent. Unrecognised images are hallucinated as frequently as or more so than familiar ones (Table 1; Cole 1992). There is often a stereotyped or repetitive quality to the images. Commonly, the same image repeats itself on different occasions, though over time, many patients will experience a range of hallucinatory images. There is generally movement, although this is often stereotyped and restricted. The images rarely interact with or respond to the environment. The image is usually whole and sharply focused. It is normal sized or unusually small with a normal or unusually vivid colour. If there is distortion, this is usually of the face with a consistent exaggeration of the mouth and eye areas (ffytche & Howard 1999; Frucht & Bernsohn 2002).

RCVH are often associated with hallucinations in other sensory modalities at other times (Ballard et al. 1999;

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Table 2. *Risk factors for recurrent complex visual hallucinations*

PATIENT GROUP	Sleep disorders	Cognitive impairment	Poor vision	Other risk factors *Nonrisk factors*
Parkinson's disease	Daytime somnolence[4], *sleep disturbance*[4]	Cognitive impairment[1,2,3,4], subsequent dementia with Lewy bodies, or Alzheimer disease[11]	Visual acuity[1,2], poor colour, and contrast discrimination[18]	Depression[1,2,3], disease severity[1,2,3,4], disease duration[2,4], age[4], previous psychiatric disease[11], *history of psychiatric disease*[1], *dose of anti-Parkinsonian treatment*[1,2,3,4], *duration of treatment*[1], *duration of disease*[1], *depression*[3]
Alzheimer's disease		More rapid decline[5], cognitive impairment[7,8], visual agnosia[19]	Relative occipital atrophy[6], visual acuity[7,19]	
Dementia with Lewy bodies		Cognitive impairment[8], overlapping figure identification[16], variability in attentional reaction time[17], *cognitive impairment*[3]	Occipital hypometabolism and preserved posterior temporal/parietal metabolism[10]	Absence of occipital white matter hyperintensities[9], *age*[3], *age at onset*[3], *anti-Parkinsonian medication*[3], *depression*[3]
Dementia (mixed diagnoses) with or without hallucinations	Nighttime disturbance[12],	Clock drawing[12], CAMCOG object recognition[12], diagnosis of DLB[12,15], diagnosis of not AD[12], *MMSE*[12], *total CDR*[12]	Near and far visual acuity[12,15,27], ambient illumination[12]	Age[15,27], female[27] *age*[12], *sex*[12], *illness duration*[12]
Eye disease	Fatigue[26]	Cognitive impairment[14,23], stroke[14]	Bilateral sequelae[13,30], bilateral visual impairment[14,31], acute onset of visual loss[14]	Living alone[14], loneliness[12], low extraversion[29], high shyness[29], female[28,30], level of disability[30], emotional distress[30], age[31], *history of psychiatric disorder*[14], *personality*[14]
General population daytime hallucinations	*Sleep disorders*[21]	Neurological disorders[21], dementia[22]	Poor vision[21,22]	Use of recreational drugs[21], anxiety[21], psychosis[21], depression[22], vivid day dreams[25], *bipolar disorder*[21], *alcohol use*[21], *hypnotics*[21], *depression*[21], *adjustment disorder*[21]
General population hypnagogic and hypnopompic hallucinations	Sleep disorders[20]			Anxiety[20], depression[20], psychosis[20]
Schizophrenia including paraphrenia			Poor vision[24]	

Italics indicate a nonsignificant relationship. Sources: (1) Holroyd et al. (2001); (2) Barnes & David (2001); (3) Aarsland et al. (2001a); (4) Fenelon et al. (2000); (5) Wilson et al. (2000); (6) Holroyd et al. (2000); (7) Chapman et al. (1999); (8) Ballard et al. (1999); (9) Barber et al. (1999); (10) Imamura et al. (1999); (11) Goetz et al. (1998a; 1998b); (12) Murgatroyd & Prettyman (2001); (13) Brown & Murphy (1992); (14) Holroyd et al. (1992); (15) Ballard et al. 1995a; (16) Mori et al. (2000); (17) Wesnes et al. (2001); (18) Diederich et al. (1998); (19) Holroyd & Sheldon-Keller (1995); (20) Ohayon et al. (1996); (21) Ohayon (2000); (22) Ostling & Skoog (2002); (23) Pliskin et al. (1996); (24) Howard et al. (1994); (25) Morrison et al. (2002); (26) Menon et al. (2003); (27) O'Reilly & Chamberlaine (1996); (28) Shiraishi et al. (2004); (29) Teunisse et al. (1998, 1999); (30) Scott et al. (2001); (31) Teunisse et al. (1995).

DWB, dementia with Lewy bodies; AD, Alzheimer's disease; MMSE, Mini Mental Status Examination; CDR, cognitive drug research.

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Table 3. *The phenomenology of recurrent complex visual hallucinations*

	Phenomenology																															
	Duration	Reaction			Appearance					Environment															Movement							
DISORDER	Lasts minutes	Neutral or positive emotion	No interaction with patient	Insight	Coloured	Normal or small	Sharply formed	Part of visual field	Complete image	Occurs at specific time	Occurs in specific place	Common in evening	Poor light	No immediate trigger	Associated with inactivity	Not associated with sleep	Fits in with Context	Mainly open eyes	Intrinsic movement	Image moves around	Image moves with eyes	Disappears with eye movement										
Eye disease	√[1,4,14,28]X[18,19]	√[4,19,6,27]X[17]	√[1,5]	X[3,9]√[19]	√[1,4,14,19,6,28]	√[1,2,14,19]	√[1,4,17,18,6,28]	√[1,7,13,17,28]X[14]	√[1,4,6]	X[14,27]	√[4]	√[4,13]X[27]	√[4]	√[4,18]	√[4]	√[4,28]	√[4]	√[4,18,27]	√[4,6,17]X[18]	X[4]√[6]	X[4]√[17]	X[17]√[14]										
Stroke	√[14]			√[26]	X[14]	√[14]	√[14]	√[14]	√[26]	X[14]		√[6]							X[14]			√[10,14]										
Psychosis		X[8,5]√[2,3]		√[8,20]	√[13]		√[8]		√[20]				√[8]	√[8]	√[8,9]X[13]		X[8]√[5]	√[5]	√[8]		X[8]										
Peduncular hallucinosis	X[14,13]	√[15]		√[15]	√[15]		√[15]	√[13] X[14]				√[13,14]							√[15,17]	√[15]											
Dementia with Lewy bodies	√[15,25]	√[25]			√[25]	√[25]	√[25]	√[13,25]				X[25]	X[25]	√[25]		√[25]		√[25]	√[25]			X[25]									
Parkinson's disease	√[21]X[22]	√[12,24]		√[23]	X[21]	√[22]		√[21]				X[23]√[24]	√[21]					√[21]	√[21]			X[21]									
Alcohol		X[21,2]				√[13]																									
Thalamic hallucinosis	√[11]							√[11]																							
Deep brain stimulation		√[16]			√[16]			√[16]			√[16]								√[16]	√[16]											
Total √ reports	9	11	2	6	10	8	10	12	5	0	2	6	3	4	3	3	2	6	9	3	1	3									
Total X reports	5	5	0	2	2	0	0	2	0	3	0	3	1	0	1	0	1	0	2	1	2	3									

Sources are a mixture of quantitative and qualitative descriptions. To combine these, we have used a quantitative distinction between whether a feature occurs 50% or more of hallucinations (√), or less than 50% (X), and a qualitative report that a feature is characteristic (√) or not (X) of hallucinations in that disorder. Sources: (1) Nesher et al. (2001); (2) Deiker & Chambers (1978); (3) Pliskin et al. (1996); (4) Teunisse et al. (1996); (5) Asaad & Shapiro (1986); (6) Schultz & Melzack (1993); (7) Fernandez et al. (1997); (8) Gauntlett-Gilbert & Kuipers (2003); (9) Delespaul et al. (2002); (10) Vaphiades et al. (1996); (11) Noda et al. (1993); (12) Godwin-Austin (1999); (13) Manford & Andermann (1998); (14) Kolmel (1993); (15) Risser & Powell (1993); (16) Diederich et al. (2000); (17) Santhouse et al. (2000); (18) Schultz et al. (1996); (19) Paulson (1997); (20) Zarroug (1975); (21) Barnes & David (2001); (22) Holroyd et al. (2001); (23) Fenelon et al. (2000); (24) Gold & Rabins (1989); (25) Bowen et al. (unpublished data); (26) Anderson & Rizzo (1994); (27) Shiraishi et al. (2004); (28) Scott et al. (2001).

Deiker & Chambers 1978; Fenelon et al. 2000; Gauntlett-Gilbert & Kuipers 2003; Goetz 1999; Holroyd et al. 2001; Howard et al. 1994; Needham & Taylor 2000; Noda et al. 1993; Ohayon 2000; Simard et al. 2003; Zarroug 1975). Thus, people with visual hallucinations may have auditory hallucinations of voices, but it is very rare to hallucinate a figure that talks (Gauntlett-Gilbert & Kuipers 2003).

4.1.2. Time and place. Episodes of RCVH tend to be of the order of minutes, rather than seconds or hours, with an abrupt onset with no apparent trigger. Offset is equally sudden. Sometimes they disappear on changes in the visual environment, though often again there is no apparent cause. They more rarely occur with eyes closed (Barnes & David 2001; Melzack 1991; Menon et al. 2003; Schultz & Schultz et al. 1996; Shiraishi et al. 2004; Teunisse et al. 1996).

By definition, the commonest hallucinations of normal life, hypnopompic and hypnagogic, are associated with falling asleep or waking. Similar associations with times of low arousal (sitting or otherwise resting) have been reported in Parkinson's disease (Fenelon et al. 2000), schizophrenia (Delespaul et al. 2002), and eye disease (Lalla & Primeau 1993), though in schizophrenia as in delirium, hallucinations have also been reported to be accompanied by over-arousal (Manford & Andermann 1998). Associations with times of low (as opposed to bright or absent) illumination have been reported in dementia (Murgatroyd & Prettyman 2001) and eye disease (Lalla & Primeau 1993; Teunisse et al. 1996), and it seems plausible that hypnagogic and hypnopompic hallucinations may also be occurring at times of low illumination.

The time of day of hallucination may be consistent within the individual, though most often it is not. In contrast, RCVH tend to occur in the same location, mostly in the house or looking out of the house. As an example, patients with dementia often report visitors who only appear in their living room. Although this may partially be a function of the amount of time spent in each location, it is striking that once the patient moves to a new environment, the hallucinations disappear (Cole 1992). The image usually appears in a contextually correct location – a person who is sitting in a chair rather than floating on the ceiling – and with the correct orientation – an upright rather than inverted face, for example.

Hallucinatory images occur in the focus of the visual field and do not generally disappear when attended to (Kolmel 1993; Manford & Andermann 1998; Santhouse et al. 2000). The hallucinatory image is seen against the background of the existing visual scene more often than is an image of a person and background filling the whole visual field (Barnes & David 2001; Manford & Andermann 1998; Scott et al. 2001). Although these latter, panoramic, hallucinations are described in eye disease (ffytche & Howard 1999; Scott et al. 2001; Teunisse et al. 1995; 1996), they are in the minority. It may be that in a person with no effective vision, there will be no existing visual scene to act as the background to a nonpanoramic hallucination.

5. Requirements for a general model

A good general model should account for who hallucinates, what they see, and when and where they see it. Thus, at a minimum, a general model of RCVH has, in our view, to be applicable to the pathological states of dementia, delirium, schizophrenia, and eye disease. It should also account for the induction and treatment of RCVH by pharmacological manipulations. It needs to predict why nonpathological hallucinations occur on the borders of sleep. It has to explain the associations within disorders with poor vision, disturbed alertness, and intellectual impairment. Finally, it needs to account for the phenomenology of RCVH; for the frequency of hallucinations of people and animals; for their abrupt onset and offset, and their movement; for temporal and situational regularities where they exist; and last, for their extinction with eye closure.

6. Existing models

A number of candidate models have been put forward based upon the pathology in particular disorders in which hallucinations occur. These have mostly been developed in parallel, with the result that there is a degree of overlap. For example, cortical irritation and more modern versions of cortical release both suggest hyperexcitability in visual cortex as a causative mechanism.

Despite each model's undoubted strengths, we feel that each faces considerable challenges when measured against the aforementioned requirements. Because none were developed with these requirements in mind, at the least all would require extension. However, beyond this, we feel that each faces the major hurdles outlined next.

6.1. Illusionary misperceptions and misidentifications

This intuitive explanation suggests that the hallucination is simply the failure to see something correctly – and hence to mistake it for something else. It is not widely supported, even by patients (Nesher et al. 2001). Two areas of evidence count against it. Misperceptions would seem most likely if objects were not at the focus of attention. However, many RCVH occur in the very centre as opposed to the periphery of the visual field (Kolmel 1993; Manford & Andermann 1998; Santhouse et al. 2000). Misperception would also suggest that rather than the experience of an image being superimposed on a background, it should take the place of another perception. The hallucination would not be of a person sitting on a chair, but of a chair turning into a person and back again. This has been reported in eye disease (ffytche & Howard 1999). In these cases, however, it appears to be a separate phenomenon that accompanies RCVH rather explains it. Thus, patients with these experiences also have more purely hallucinatory images.

6.2. Cortical irritation

This model suggests that hallucinations result from intrinsic electrical overactivity in the brain areas that contain specific image memories or representations (Levine & Finklestein 1982; Noda et al. 1993). It was developed initially to account for visual hallucinations in temporal lobe epilepsy and drew on Penfield's work on the effects of stimulation of that area (e.g., Penfield & Perot 1963). As previous reviewers have concluded, however, it has a range of limitations as a general model (Brasic 1998; Manford & Andermann 1998; Schultz & Melzack 1991). Penfield's initial formulation of experiential hallucinations as reactivated

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memories is at odds with the unfamiliarity of many hallucinations. Though Horowitz et al.'s later stimulation work activated a wider range of images (Horowitz et al. 1968), many of which are reminiscent of those described by people who hallucinate, this still leaves the problem of the lack of evidence for focal cortical irritation in the majority of people with RCVH (e.g., from stroke; see Anderson & Rizzo 1994; Vaphiades et al. 1996).

6.3. Cortical release and hyperexcitability or unbalanced top-down activation

Au Eong et al. (2001), Anderson and Rizzo (1994), Asaad and Shapiro (1986), Brasic 1998, Burke (2002), Cogan (1973), Fernandez et al. (1997), ffytche and Howard (1999), ffytche et al. (1998), Howard et al. (1997), Lepore (1990), Santhouse et al. (2000), Schultz and Melzack (1991), and West (1962) suggest that, in several disorders, hallucinations result from a lack of sensory input. They suggest that this results in the release of stored images. This initially drew upon what was then thought to be the inhibitory nature of stimulus-driven, bottom-up visual processing with a lack of inhibition-releasing spontaneous activity. More recent conceptualisations (e.g., Burke 2002) suggest that a lack of input leads to chronic hyperexcitability. In a development of these ideas, Manford and Andermann (1998) and Stoerig (2001) brought together a wide range of different causes of visual hallucinations by suggesting that they perturbed diverse aspects of the visual system, although, as with other models in this class, the common result was a hyperexcitability or disinhibition of image-containing cortex.

Approaching this from the other end of visual processing, Grossberg (2000) suggests that, within adaptive resonance theory (ART), hallucinations are caused not by a lack of bottom-up inhibition but by an excess of excitation from top-down attentional processes. In general, these top-down excitations are not enough to spontaneously activate images, unless the person wills it. However, Grossberg argues that, on occasions, they become tonically hyperactive with incorrectly activated images (hallucinations) as the result.

There are strengths in these models that invoke cortical release. They are able to account for the content of RCVH by the cortical areas that are released (ffytche et al. 1998; ffytche & Howard 1999; Santhouse et al. 2000). ART may be able to explain the recurrent features of hallucinations by linking activation of the hallucinatory image to the context in which the prototype image was learnt. However, this class of models struggles particularly in predicting who has complex hallucinations. Dysfunction of visual input (eye disease, occipital lesions, or sensory deprivation) alone (Fig. 1), and isolated failures of attentional regulation due to stroke (Chemerinski & Robinson 2000; Rabins et al. 1991) or frontotemporal dementia (Bathgate et al. 2001) are associated with rates of RCVH in, at most, the 10–15% range. This is well below that seen in some forms of dementia or delirium. As we will show, it may be that both sensory release and top-down activation are necessary, but neither in itself is sufficient to cause high rates of RCVH. Returning to the double dissociation between simple and complex hallucinations and the relatively high rates of simple hallucinations in eye disease and sensory deprivation, it may be that the disinhibitory effect of lack of sensory input more successfully accounts for simple hallucinations.

6.4. Dream intrusion

Dream intrusion suggests that hallucinations are the intrusions of dream images into waking or semi-waking states (Arnulf et al. 2000; Asaad & Shapiro 1986; Manni & Mazzarello 2001; Manni et al. 2002; Nomura et al. 2003; Onofrj et al. 2002; Pappert et al. 1999). It has a long history as an explanation, dating back to L'Hermitte's initial descriptions of peduncular hallucinosis, though there is almost an equally long history of disagreement (for discussions, see Asaad & Shapiro 1986; Risser & Powell 1993).

In support of this as a general explanation, RCVH in dementia and Parkinson's disease have been reported to be associated with periods of sleep or disturbed alertness; fatal familial insomnia, delirium, and narcolepsy are all characterised by primary impairments in alertness or sleep; and virtually all non-pathological hallucinations occur between sleep and full wakefulness.

We see three major challenges to dream intrusion as a general explanation. First, RCVH are less common in some disorders with primary impairments of alertness (narcolepsy without cataplexy and delirium) than in other illnesses in which disordered alertness, though common, is not an invariable feature (dementia with Lewy bodies and vascular dementia; Fig. 1). Second, within specific disorders, there is not an invariable relationship between sleep disturbance and RCVH. Thus, RCVH in narcolepsy is associated more with cataplexy than sleep disorder per se (Aldrich 1996); and within peduncular hallucinosis, a significant minority of patients do not have sleep abnormalities (Risser & Powell 1993). In Parkinson's disease, although sleep disorder and RCVH both occur, they do not necessarily occur in the same patient or at the same point in the illness (Arnulf et al. 2000; Manni et al. 2002; Nomura et al. 2003; Onofrj et al. 2002). Third, dreams and RCVH are phenomenologically distinct. Dreams fill the whole visual field, with the dreamer being a participant in the action. In contrast, visual hallucinations occupy only the centre of the visual field, with the hallucinator being an observer. Even when content is similar (Nomura et al. 2003), people who experience both are well able to tell them apart (Arnulf et al. 2000; Cole 1999).

6.5. Interactive and information-processing models

Asaad and Shapiro (1986), Brasic (1988), Gold and Rabins (1989), and Schultz and Melzack (1991) describe a number of solely psychological theories to account for RCVH. Causal theories are mainly, though not exclusively, psychodynamic and sociological. They argue that visual hallucinations arise from trauma-induced breakdowns in ego boundaries, or a culturally influenced exaggeration of the normal human propensity to hallucinate. On the positive side, their dependence on internally generated images is supported by evidence that spontaneous and volitional images are a normal feature of many people's lives (Horowitz 1967; McKelvie 1994). The emphasis on the role of expectancies and past experience is consistent with evidence that childhood and adult trauma is a risk factor for RCVH (Read et al. 2003) and that vivid daydreaming is associated with visual hallucinations in non-patients (Aleman et al. 1999; 2000; Morrison et al. 2002). Furthermore, flashbacks incorporating visual experiences are characteristic of posttraumatic stress disorder (American Psychiatric Association 1994). Bereavement may be followed by visual hallucinations of the deceased, though more commonly in other modalities

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and perhaps not more frequently in the general population of a similarly old age (Grimby 1993; 1998; Rees 1971; Schneck 1990; Wells 1983), and there is some evidence that hallucinations interpreted as hauntings are associated with expectancies congruent with this (Lange et al. 1996). There are also reports of emotionally significant experiences influencing the content or interpretation of, and hence emotional reaction to, some hallucinations (Needham & Taylor 2000; Schultz & Melzack 1993). This is not the case for the majority of hallucinations (Teunisse et al. 1996).

Overall, given the preponderant associations of RCVH with organic disease (Figs. 1 and 2), and that it is so rare in psychologically normal, or clinically anxious or depressed people (outside of sleep-wake transitions), it seems improbable that purely psychological factors cause more than a minority of hallucinations, though they may affect the interpretation and emotional reaction to them (Collerton & Dudley 2004).

In psychosis, difficulties with explanations that rely on a single cause have led to the development of models in which several factors can interact. In a well-developed information-processing model, Bentall and coworkers (Bentall 1990; Slade & Bentall 1988) suggest that visual hallucinations result from mistaking an internally generated image for one based on an external reality as a consequence of an impaired reality monitoring: a model analogous to models of auditory hallucinations that suggest these are misidentified internal speech (e.g., McGuire et al. 1996). This image may be generated without awareness and appear to intrude into consciousness. They suggest this becomes more likely if there is high arousal, a predisposition to confuse reality with imagination, a poor environmental signal-to-noise ratio, a context that encourages hallucinations, and reinforcing changes in arousal associated with the hallucination. Morrison and colleagues (Morrison 2001; Morrison et al. 2002; 2003) have elaborated on this to account for the relationship between with traumatic experience and hallucinations. Extending this to Parkinson's disease, Barnes et al. (2003) suggest that these mistakenly identified images result from a combination of impaired object perception and poor source monitoring in episodic memory.

The suggestion that the primary cognitive error is in the misidentification of an internal image seems to us to conflict with the evidence that about half of the people are aware that they are hallucinating. Granted that the misidentification might be nonconscious, it needs to be demonstrated how it has little apparent relationship to conscious awareness of unreality, especially when volitional images and dreams are readily identified as such, and when there is no other apparent differences between hallucinators with and without awareness. Additionally, although subjective visual vividness is related to reported hallucination proneness, imagery performance is not (Aleman et al. 1999; 2000).

Horowitz's perceptual nidus theory (Horowitz 1975) does not depend upon this mistaken identification. It suggests (as we later do ourselves) that the primary pathology lies in the generation of images rather than their tagging as internal or external. He suggests that hallucinations occur when there is a combination of an ambiguous relationship between an internal image and reality (the perceptual nidus), in combination with a template of expectancy (derived from psychoanalytic drives and other wishes), and an active memory or fantasy image. This shares several central features with our PAD model, though it was only after we developed it that we became aware of Horowitz's work.

Perhaps the greatest problem for these models as they stand at present is in accounting for the variations in the frequency of RCVH across disorders. There seems no a priori reason why images should be generated or mistaken less frequently in, for example, eye disease than in dementia with Lewy bodies, or that the perceptual nidus would systematically vary across disorders.

Recent biological models of psychosis have focussed on the role of the thalamus in coordinating the multiple brain areas that subserve attention and perception (e.g., Behrendt & Young 2004; Lee et al. 2003; Pelaez 2000). They suggest that thalamic dysfunction creates a stable perception that incorporates incorrect elements. Though attractive in that they can reconcile the need for multiple factors interacting, these models are at odds with the lack of relationship between thalamic dysfunction and rates of RCVH across different disorders (Collerton & Perry 2004). Thus, massive but restricted thalamic damage due to infarcts (del Mar Saez de Ocariz et al. 1996) or fatal familial insomnia (Gallassi et al. 1996; Tabernero et al. 2000) is not generally associated with RCVH, though isolated cases have been reported (Noda et al. 1993). Conversely, we show later how thalamic dysfunction need not be present in disorders with high rates of RCVH.

7. The Perception and Attention Deficit (PAD) model

Based on the foregoing analysis, we conclude that the existing models of RCVH have specific strengths, but all have limitations as general models. This led us to develop a new model. We were guided by two features of RCVH: (1) the occurrence of the hallucination at the focus of visual attention in an otherwise unchanged scene, and (2) the cognitive and pathological characteristics of the disorder with the most consistent evidence for the highest levels of RCVH – dementia with Lewy bodies. (The finding that narcolepsy with cataplexy has equally high rates rests upon a single report from Aldrich 1996.) Exploring these led us to propose that most cases of RCVH are a result of combined attentional and visual perceptual impairments interacting with scene representations to produce the activation of incorrect but environmentally expected perceptual proto-objects.

7.1. Normal scene perception

Cognitive psychology models of scene perception (e.g., Biederman 1972; Biederman et al. 1973; 1974; 1982; 1983; Henderson & Hollingworth 1999; 2003a; 2003b; Rensink 2000a; 2000b; 2002) propose that the subjective experience of a consistent, whole visual world is a construction based upon interactions between abstracted top-down attentional, perceptual, and mnemonic processes and bottom-up sensory processes, with the former generally the more influential in subjective perception (Fig. 3). In parallel, neuropsychological models of selective visual attention and frontal lobe function (e.g., Desimone & Duncan 1995; Miller & Cohen 2001), and of the ventral visual stream and object perception (e.g., Grill-Spector 2003; Vecera 2000), have developed similar divisions. They also require abstract, top-down representations – attentional, feature, or

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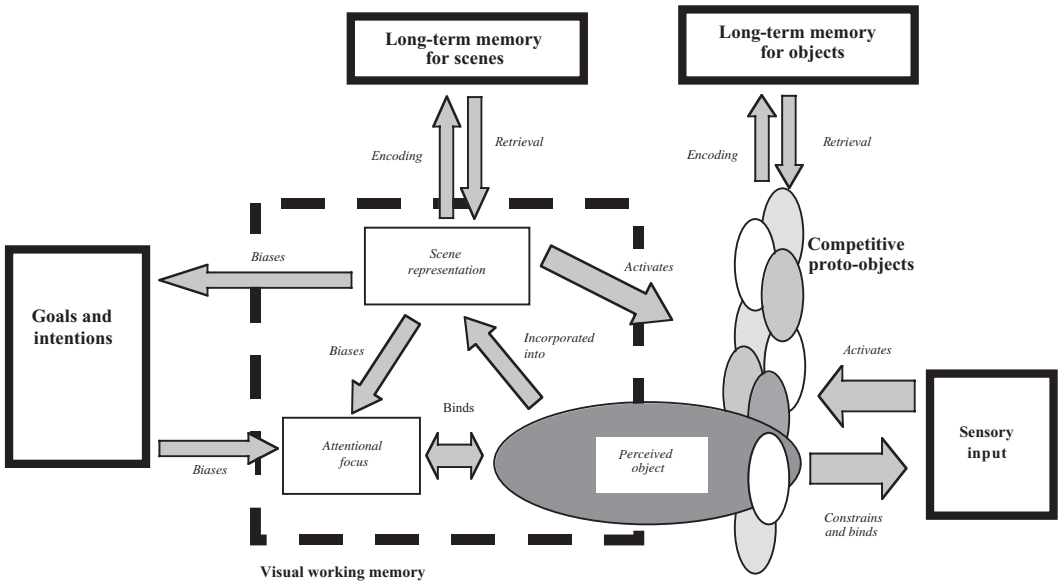

Figure 3. A model of scene perception. This model is the integration of several aspects of the perception of scenes and of objects within those scenes. It draws heavily on Rensink's triadic architecture (Rensink 2000a; 2000b; 2002), Henderson and Hollingworth's visual memory theory (Henderson & Hollingworth 2003a; 2003b), and Desimone and Duncan's biased competition account (Desimone & Duncan 1995; Miller & Cohen 2001; Vecera 2000; Vecera & Behrmann 2001). It is described as if these processes are separable, though this may be more conceptual than real (Peterson & Rhodes 2003; Tarr 2003).

object templates. These are activated by, but also act to bias processing of, sensory and mnemonic information towards specific subjective perceptions. Thus, subjective perception is the result of dynamic reciprocal interactions among external sensory input, internal object and scene representations, and goal-directed attention (Driver et al. 2001; Frith 2001; Scholl 2001; Vecera & Behrmann 2001; Wolfe et al. 2003).

As external sensory input changes, it either activates a number of new, potentially "seen" proto-objects, or modifies those already activated. These proto-objects are not in conscious awareness. They are holistic (Farah et al. 1998) or part-based abstracted object representations (Peterson & Rhodes 2003; Tarr 2003) that are segmented from visual information and act as candidate objects for further processing (Driver et al. 2001; Wolfe et al. 2002). They are equivalent to templates in Desimone and Duncan's biased competition account (Desimone & Duncan 1995; Miller & Cohen 2001; Vecera 2000; Vecera & Behrmann 2001).

These proto-objects are in mutual competition for further processing. Top-down or bottom-up biasing information will influence this competition to allow one to enter conscious awareness and be *seen*. Thus, highly salient physical properties of the visual stimulus created by the object – colour, brightness, contrast, for example – can produce a bottom-up bias that allows unattended objects to enter awareness (Rensink's low level visual System I; Frith 2001; Tarr 2003). Similarly, top-down biasing information from familiarity of the object, individual goals and expectancies, and spatial attention will influence the speed and accuracy of object awareness (reviewed in Vecera 2000).

Top-down activation of a number of proto-objects may come from a mnemonic representation of the visual scene (Biederman's scene schema, Rensink's nonattentional setting System III, Henderson & Hollingworth's Scene Representation). Though exact conceptualisations differ, this is an abstract, relatively stable, relatively sparse, noniconic, nonsensory representation reflecting a specific environment. Elements of this are built up in long-term memory over successive attended perceptions of scenes (Chun & Nakayama 2000; Henderson & Hollingworth 2003a; 2003b; Irwin & Zelinski 2002; Shinoda et al. 2001). It contains gist and semantic information about the scene as a whole, as well as details on object shape and layout (Henderson & Hollingworth 2003a; 2003b; Rensink 2000a; 2000b; 2002). It also has the properties of a template in the sense that it biases sensory processing, though different conceptualisations locate this pre- and post-object recognition: Henderson and Hollingworth suggest there is little influence on object recognition per se, whereas Biederman assigns a direct, and Rensink, a more indirect, role in this.

This scene representation, together with ongoing goals and intentions, also influences dynamic top-down attentional processes (Chun & Nakayama 2000; Clark 2002; Humphreys & Riddoch 2001/2002; O'Regan et al. 2000). Attention is the primary mechanism for biasing competition among proto-objects via an increase in signal to internal noise (Lu & Dosher 1998). This induces further segmentation and attentional binding of object features and a relatively stable "seen" object (Rensink's attentional object binding System II; Delvenne & Bruyer 2004; Driver et al. 2001; Treisman & Gelade 2001; Wheeler & Treisman 2002). Thus, seen objects are behaviourally relevant but temporally limited (Beck & Levin 2003). Once active, object representations both bias lower-level sensory processing (Peterson 1999; Vecera & Behrmann 2001) and are incorporated into the higher level scene representation.

The interplay of these processes is closely, but not exactly, related to visual working memory (de Fockert et al. 2001; Delvenne & Bruyer 2004; Henderson & Hollingworth 2003b; Irwin & Zelinski 2002; Scholl 2001; Wheeler & Treisman 2002).

7.2. The characteristics of dementia with Lewy bodies

In a meta-analysis of the cognitive impairments found in dementia with Lewy bodies (Collerton et al. 2003), we identified a cognitive profile characterised by uniquely severe impairments in both attentional/executive performance and visual object perception. Thus, the disorder with the highest rates of RCVH also has the most severe combination of impairments in two key functions that must interact to produce normal scene perception. Combining this neuropsychological finding with evidence from the pathology of dementia with Lewy bodies and the induction of RCVH by cholinergic manipulations, we formulated a general model for RCVH.

7.3. Summary of the PAD model

We suggest that, within scene perception, a hallucination is experienced when an incorrect proto-object is bound in the attentional focus of a scene. This is generally when the visual system is constrained by a combination of impaired attentional binding and poor sensory activation of the correct proto-object, in conjunction with a relatively intact scene representation that biases perception towards an incorrect image. Either impaired attention or impaired sensory activation alone will rarely produce hallucinations. The relationship between the correct and the incorrect proto-object distinguishes a hallucination from an illusion or a misperception; the more distant the relationship, the more hallucinatory the experience.

From this, we suggest that:

1. The frequency of RCVH varies with the frequency of the coexistence of attentional dysfunction and object perception impairments.[2]

2. The phenomenology of RCVH – what is hallucinated, and where and when – primarily reflects the nature of scene perception, in particular, the role of scene-based expectations in influencing the attentional focus (what), and environmental and temporal cues in triggering a scene representation that biases processing towards a hallucination (where and when).

3. Object-based attention depends primarily upon the function of lateral frontal cortex, and object perception depends primarily upon the ventral visual stream. Thus, disorders associated with high levels of RCVH will have a common end stage of both lateral frontal cortex and ventral stream dysfunction. This may be due to intrinsic or extrinsic pathology.

Sections 7.4 to 7.6 demonstrate how the PAD model is consistent with the evidence that highlights the limitations of previous models.

7.4. The relationship between the frequency of RCVH and the coexistence of attentional and perceptual impairments

7.4.1. Associations of RCVH with disease and other states. If the PAD model is correct, there should be a consistent relationship between the severity of attentional and perceptual impairments and the frequency of RCVH across relevant disorders. Neither attentional nor perceptual impairments alone should be associated with high levels of RCVH.

The strongest test of this postulated relationship would be to directly relate attentional and perceptive impairments within scene perception to the occurrence of RCVH. However, such data are not yet available. As an interim measure, we set out to test whether lower rates of RCVH were related to lesser impairments in broad attentional and perceptual function. We plotted rates of RCVH against the severity of attentional and visual perceptual impairment across those disorders for which we could locate data (Fig. 4). We first did this for the disorders included in our dementia with Lewy bodies meta-analysis, then extended it to include other disorders on which we could find comparable data – vascular dementia and Parkinson's disease dementia. Across these disorders, there is the strong correlation that the PAD model requires. At least two potential objections arise to this finding. It is clear that within this data set, attentional and visual perceptual impairments closely covary in severity as a consequence of averaging data from tasks which are both attentional and visual-perceptual. It could be argued therefore that either alone could be sufficient, with the relationship with the other being correlational rather than causal, or that both are reflections of another shared factor. However, as we noted in section 6.3, neither attentional nor visual impairments alone are associated with high levels of RCVH. Nor are RCHV strongly related to other factors (general verbal as opposed to nonverbal impairment, or overall severity of impairment), suggesting a degree of specificity in these cognitive domains. It might also be that the unusually strong relationship is an artefact of the meta-analysis. For example, dementia with Lewy bodies is diagnosed by both the presence of visual hallucinations and attentional fluctuation. Hence, they might appear to coexist as a reflection of patient selection bias. This cannot be rejected as a partial explanation, but if this bias were to account for the findings in other disorders, this would need to systematically vary across other neurodegenerative disorders. We do not consider this likely, but it needs to be tested by direct assessments of hallucinations and cognitive performance across disorders.

In support of evidence relating the general severity of attentional and visual perceptual impairments to the risk of RCVH across disorders, are the relationships within different neurodegenerative disorders. In dementia with Lewy bodies, RCVH has been separately related to the severity of attentional impairment (McKeith et al. 2004; Wesnes et al. 2001) and the severity of visual perceptual difficulties (Mori et al. 2000; Simard et al. 2003). Furthermore, the characteristic intellectual impairments of this disorder may predate the occurrence of hallucinations (Ferman et al. 2002). Barnes et al. (2003) showed a combination of impaired object perception and poor source monitoring in hallucinating patients with Parkinson's disease. To maintain consistency with the PAD model, this difficulty in source monitoring could result from dysfunctional attentional processes (Henkel et al. 1998).

In relation to the other disorders to which a general model of RCVH has to apply, the evidence, albeit even less direct, is not against PAD as a potential model.

Although the evidence is less systematic, poor performance on tests of attention and visual perception are also the norm in delirium (Hart et al. 1997; Mach et al. 1996; O'Keeffe & Gosney 1997) and in schizophrenia (Bozikas et al. 2002; Cuesta et al. 1998; Davidson et al. 1996; Gabrovska et al. 2002; Gold et al. 1999; Hoff et al. 1996; 1999; Park et al. 2002; Sanfilipo et al. 2002). In direct comparisons between patients with Alzheimer's disease and schizophrenia,

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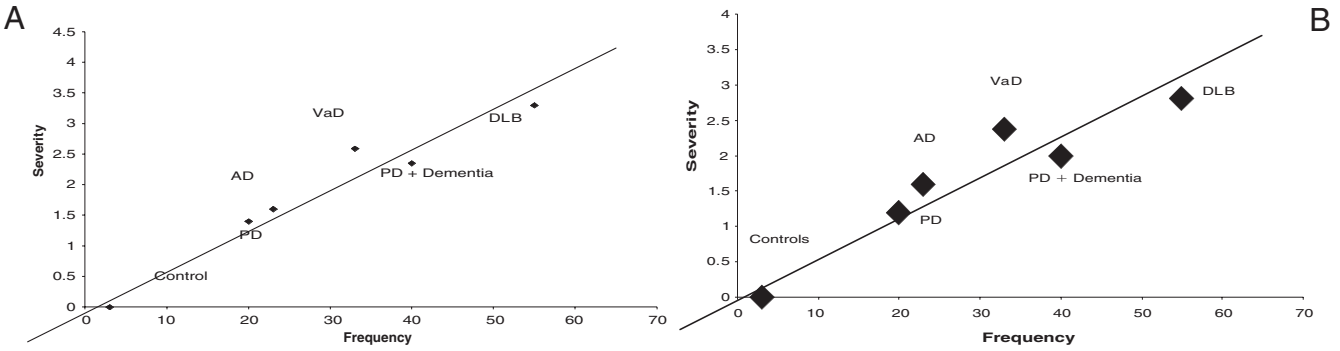

Figure 4. Relationship between frequency of visual hallucinations and severity of (**A**) visual perceptual and (**B**) attentional impairments in neurodegenerative and dementing illnesses. The frequency of RCVH for each disorder is taken from Figure 1. Factor analysis of over 160 tasks used in different neuropsychological studies of these diseases identified four factors: general verbal/nonverbal impairment, attentional/executive impairment, visual perceptual impairment, and verbal memory impairment. The severity of impairment is an inverse variance weighted average of effect sizes on a factor. Full details of the methodology are in Collerton et al. (2003; erratum Collerton et al. 2004). Visual perceptual impairment, $r^2 = 0.92$, $p < 0.01$, and attentional impairment, $r^2 = 0.88$, $p < 0.01$, are both reliably related to the frequency of visual hallucinations. However, overall severity of impairment, $r^2 = 0.52$, $p > 0.1$, general verbal/nonverbal impairment, $r^2 = 0.15$, $p > 0.4$, or severity of verbal memory impairment, $r^2 = 0.63$, $p > 0.05$, were not reliably related to the frequency of hallucinations in this data set. Data for Parkinson's disease (PD, averaged from three studies) and Alzheimer's disease (AD, 10 studies), and dementia with Lewy bodies (DLB, 10 studies) are from Collerton et al. (2003). Data for vascular dementia (VaD) were calculated from five studies referenced in Looi and Sachdev's (1999) systematic review of the cognitive profile of vascular dementia. Data for Parkinson's disease plus dementia were calculated from seven studies identified through Medline and PsycInfo (Ballard et al. 2002; Goldman et al. 1998; Huber et al. 1986; McFadden et al. 1996; Piatt et al. 1999; Soininen et al. 1992, Starkstein et al. 1996).

the patients with schizophrenia had equal attentional and greater visual perceptual impairments (Davidson et al. 1996) consistent with the higher rates of visual hallucinations in the latter illness. The hallucinations that result from deep brain stimulation are also associated with impaired attentional and visual perceptual performances (Saint-Cyr et al. 2000; Trepanier et al. 2000). However, comparisons within these disorders between hallucinators and non-hallucinators need to be made to directly test the model.

In acquired eye disease, poor performance on cognitive tests and the occurrence of stroke disease, both of which might be expected to increase the risk of attentional impairments, are risk factors for RCVH (Table 3). As a corollary, low illumination levels or poor vision (both of which will impair visual recognition) are risk factors for RCVH in dementia. The association with disturbed alertness may reflect the close relationship between this and attention.

The PAD model needs to account for the association of hallucinations with the borders of sleep. The dream intrusion model suggests that some of the features of sleep account for the presence of hallucinations just before or after sleep. However, other possibilities exist that would be consistent with the PAD model. First, it is likely that the transition from sleeping to waking dysregulates the attentional system. Second, sleeping tends to take place at the same time and in the same place each day, often in low illumination. These factors would not only provide the consistent context that we suggest leads to hallucinatory scene representation activation but also impair visual function.

Post-bereavement and other psychologically induced hallucinations may reflect the goal-directed nature of active attentional perception. It may be that difficulties in accepting the loss may potentiate expectations from specific scene representations to engender a purely top-down activation of an image (Schneck 1990). In support of this, the prevalence of post-bereavement hallucinations rises with the length of the relationship with the deceased (Rees 1971), and a better quality of the lost relationship and present loneliness predict hallucinations (Grimby 1993; 1998). These may be some of the uncommon top-down hallucinations. However, given that there is no evidence on risk factors for post-bereavement and other experience-engendered hallucinations, we cannot rule out impairments in sensory or object-perception processes.

7.4.2. Effects of cholinergic manipulations on attention and object perception. There is an extensive literature on the cognitive effects of anticholinergic drugs summarised by Everitt and Robbins (1997) and Ebert and Kirch (1998). Impaired performance on virtually all tests of alertness and attention following reduced cholinergic function is well established (reviewed by Beelke & Sannita 2002; Collerton 1986). Effects of cholinergic antagonism in many aspects of vision have been reported, including visual acuity, tracking performance, stereopsis, and spatial localisation (Caldwell et al. 1992; Fisher 1991; Kobrick et al. 1990; Meador et al. 1993; Mentis et al. 2000; Nobili & Sannita 1997; Penetar et al. 1988). In addition, cholinergic antagonists impair performance on simple and complex visual recognition and visual spatial tasks (Bentley et al. 2004; Dalley et al. 2004; Flicker et al. 1990; Meador et al. 1993; Obonsawin et al. 1998).

Cholinergic projections modulate the signal to noise ratio in cerebral cortex, with the effects of this depending upon the function of specific cortical areas (Everitt & Robbins 1997). In Yu and Dayan's (2002) computational model of cholinergic function, it has a specific role in modulating the interaction between top-down and bottom-up processing. Inhibition of cholinergic input gives a greater chance of incorrect pattern matching (a failure to select the correct proto-object in the PAD model) and allows the intrusion of an incorrect representation. In a similar manner to acetylcholine, dopamine is also considered to mediate a net increase in signal-to-noise ratio in select neuronal assemblies to maintain attentional focus (Dreher & Burnod 2002; Durstewitz & Seamans 2002; O'Donnell 2003). However, given that dopamine receptors are not prevalent in visual

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processing areas (whereas muscarinic cholinergic receptors are), and dopaminergic agonists induce RCVH only in conjunction with cholinergic deficits (sect. 3.2), dopamine dysfunction may only be significant when there is existing cholinergically induced dysfunction in perceptual systems.

7.5. The phenomenology of recurrent complex visual hallucinations

7.5.1. Content and phenomenology of hallucinations. We agree with others (Behrendt & Young 2004; ffytche & Howard 1999; ffytche et al. 1998) that the content and character of RCVH primarily reflects the nature of visual processing. However, we particularly stress the interaction of multiple processes within scene perception rather than the activation or release of specific visual areas.

The separation of proto-objects from sensory input (Behrmann et al. 1995; Jankowiak et al. 1992; Servos & Goodale 1995) allows the possibility that top-down biasing can activate a hallucinatory image in the absence of that input in the same manner as Grossberg's (2000) adaptive resonance theory network account suggests. Rensink's proposal that top-down processes create a seen object from a proto-object can account for why hallucinatory images are generally sharply focused and vividly coloured even in patients with poor visual ability (Menon et al. 2003). Because the PAD model suggests the intrusion of an incorrect proto-object into subjective awareness only when the correct object is not attentionally bound, this would account for the rareness of doppelgangers – duplicate but different images of a person who is present. Attentional binding of the correct proto-object would take primacy over that of an incorrect one. Polyopia, seeing multiple instances of the same image of a non-hallucinatory object, is a different phenomenon (Cutting 1997, p. 106).

Selective visual attention within scenes operates at the whole object level, with separations between the representations for, amongst others, living and nonliving objects (Humphreys & Forde 2001). This can account for why whole as opposed to partial objects are generally hallucinated – people, rather than arms or feet, for example – and why these tend to be within a restricted range of categories. It is interesting to note that the only frequently reported hallucinations of separated body parts are of heads (Santhouse et al. 2000), consistent with evidence that faces are perceived as objects in their own right with specific cortical areas specialised for their processing (Farah 2000; Farah et al. 1998; Kanwisher et al. 1997). The focus on activation of individual proto-object may account for why single, as opposed to multiple, images are the commonest hallucination.

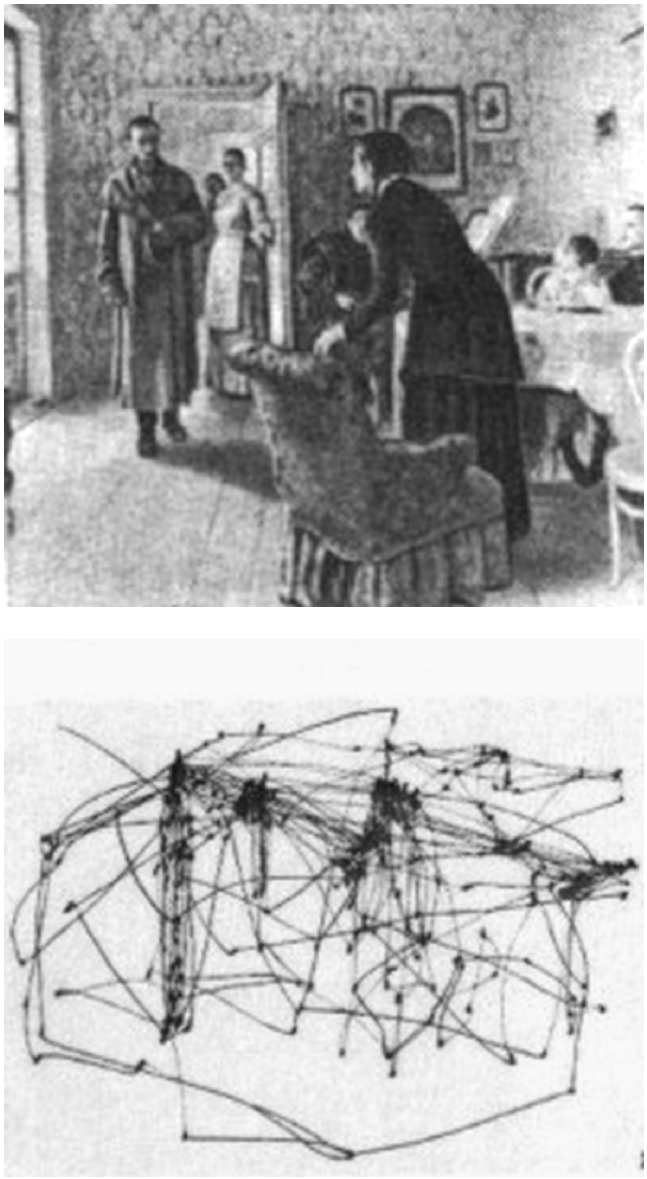

Figure 5. Illustration of eye movements indicating attention being given to animals and people in inspection of a scene. Yarbus (1967, pp. 172–79; reproduced with the permission of Plenum Press).

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The immediate behavioural relevance of attentional biasing deriving from scene templates can account for why the content of the hallucination is generally consistent with expectations from the setting in which it is seen. Studies of eye movements in scene perception (e.g., Fig. 5) suggest that attention in complex scenes is more often given to people or animals than to inanimate objects, suggesting a systematic bias towards those stimuli. In addition, specific expectancies may bias subjective perception within scenes (Henderson & Hollingworth 1999). Taken together, these may account for why people and domestic animals are the most common hallucinatory images (Menon et al. 2003), given that most hallucinations occur in the home.

A failure of attentional binding may also account for the nature of hallucinatory distortions when they occur. Those features in faces which are exaggerated are those which are normally most attended to (Fig. 6; Henderson et al. 2001). A face object is also made up of eye, nose, mouth, cheek, forehead, and other objects (Scholl 2001). If these are not bound into a whole face perception, familiarity effects (Vecera 2000) would give greater salience to those objects usually most attended to. Hence, eyes and mouths tend to be exaggerated. We would suggest that distortion might be particularly likely when proto-objects are relatively non-holistic as a consequence of being relatively unfamiliar. This might account for why, to our knowledge, distorted features are not seen on recognised faces.

Abnormally small hallucinations may be a result of the hallucinated image being unintegrated into the scene representation. Thus, as ffytche and Howard (1999) suggested, it may be perceived against an unusually close background – in the same way that a close-up projector gives a small image.

The qualities of proto-objects are not well characterised. There is the danger that we might imbue them with the qualities that are consistent with hallucinated images – though conversely, the qualities of hallucinated images may illuminate those of proto-objects. For example, one of our patients with eye disease remarked that hallucinated buildings remained in the correct perspective as he moved around their exteriors, suggesting that activated image representations are orientation independent. Proto-objects do appear to be highly variable. Generation of an image by activation of a proto-object might explain the mixture of familiar and unfamiliar images, given that it does not suggest the necessary release of specific, pre-existing, visual memories. However, further development of the distinctions within proto-objects and their relationship with episodic memory is needed before we can say this with any confidence.

Once an image is hallucinated, it may become associated with a specific hallucinatory scene representation. This increases the probability of the same image being triggered again and may account for the repetition of specific images. As particular images become part of the scene representation, they will bias perception towards themselves and away from other proto-objects. This may provide a mechanism for the reduction in the range of images with time (Holroyd & Rabins 1996). Finally, the lack of an iconic scene representation may explain why panoramic hallucinations are rare, though it does beg the question as to why they occur at all.

7.5.2. Time and place. Dynamic attentional binding is dependent upon the prefrontal representations (templates, rules, or goals) of Miller and Cohen (2001; see also Vecera 2000). Templates must both be responsive to relevant information in the environment, and resistant to irrelevant information. Thus, a dysfunctional template may fail to respond to relevant environmental information, hence allowing the abrupt activation of the hallucinatory proto-object since the correct proto-object is not bound. Attention is then captured by the hallucination, continuing the exclusion of correcting information – hence the hallucination's persistence over a matter of minutes. This can also relate to how cholinergic function can modulate signal to noise in the cortex, as discussed in section 7.4.2. If this ratio decreases, attentional focus on the correct proto-object will become more difficult.

The necessity for an environmental trigger for a scene representation (a hallucinatory scene template as it were) can account for an otherwise puzzling feature of hallucinations – that they disappear on eye closure or on complete visual loss. Volitional images are as easily evoked with open as with closed eyes (McKelvie 1995). Cortical release and dream-intrusion models would both suggest that hallucinations ought, if anything, to become more pronounced, when sensory input is further reduced. The PAD model suggests that some sensory input is necessary to activate the scene representation that biases perception and attention towards the hallucinatory image. Without a scene representation, there is insufficient top-down bias to activate a perception even with a lack of sensory activation or attentional binding of the correct proto-object.

Hallucinations may be most common in dim light since bright light improves the perception of correct proto-objects, while no light removes the cues that activate the scene representation. The extinction of complex visual hallucinations by occipital transcranial magnetic stimulation (Merabet et al. 2003), suggests that strong bottom-up influences can bias perception towards non-hallucinatory images. The reactivation of a hallucinatory template by specific environmental cues may also account for those occasions when there is consistent location or timing of hallucinations.

Since we suggest that attentional processes drive the perception (sect. 7.1), this accounts for the image being at that attentional focus. That the image is perceived within a scene representation, can account for why it does not move with eye movements. Along with Howard et al. (1997), we have located the primary visual dysfunction in the ventral (what) visual stream, allowing the possibility that the dorsal (where) stream functions relatively normally. Thus, hallucinations are generally correctly located in space.

The intrinsic movement of hallucinated images suggests that either proto-objects contain movement information or that, once activated, a perceived image activates other systems for perceiving motion. We cannot distinguish between these possibilities at present.

7.6. Relationship with specific cortical pathologies

7.6.1. Evidence that normal scene perception depends upon the interaction between lateral frontal cortex and the ventral visual stream. There is long-established neuropsychological evidence that locates executive and attentional function in the frontal lobes (Passingham 1995) and object recognition in the ventral visual stream (Farah 2000; Grill-Spector 2003). These are linked by direct and indirect projections (Fig. 7), and functional imaging suggests that

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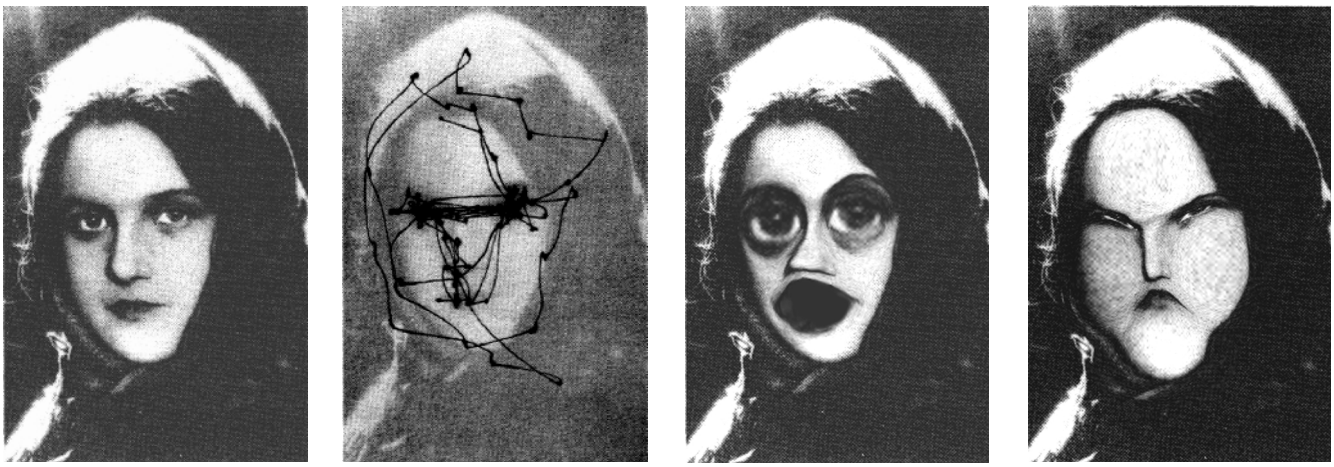

A B C D

E

Figure 6. Effects of distorting images to reflect attentional focus. Figures show the effects of distorting the original picture (Fig. 6**A**) using eye movements as an index of attention (Fig. 6**B**) to emphasize attended features (nose, eyes, and mouth, Fig. 6**C**) or unattended features (cheeks, chin, and forehead, Fig. 6**D**) (Yarbus 1967; reproduced with the permission of Plenum Press, New York). Figure 6**C** best matches descriptions of visual hallucinations. "You have stretched lips, a thick nose, and you are grinning . . . your eyes are stretched and you have big circles under them" (Santhouse et al. 2000). See also the central face (6**E**) from an artist's montage of his own visual hallucinations in Parkinson's disease (Frucht & Bernsohn 2002; reproduced by permission of Lippincott Williams & Wilkins).

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the working memory and semantic abilities thought to underlie image perception and retrieval and scene perception depend upon interactions between these frontal and posterior visual areas (e.g., Courtney et al. 1997; Fletcher & Henson 2001; Haxby et al. 2000; Ishai et al. 2000; 2002; Lumer & Rees 1999; Rowe et al. 2000; Vandenberghe et al. 1996; Wilson et al. 1993). More specifically, change blindness in scene perception, the phenomena in which a top-down scene representation overrides a bottom-up perception (Beck et al. 2001), and recognition of repeated real-world objects (Vuilleumier et al. 2002) are both associated with lateral frontal and ventral stream coactivation – among other areas.

As the PAD model demands, top-down attentional factors can bias perceptual processing in the absence of visual stimulation (Kastner & Ungerleider 2001). If frontal attentional systems are stressed by multiple tasks, there is greater activation of inferior temporal cortex and greater intrusions of incorrect information in working memory tasks (de Fockert et al. 2001). Manipulation of cholinergic function by physostigmine in normal people both improves performance on a facial recognition working memory task and decreases blood flow in prefrontal cortex and areas of the ventral visual stream (Furey et al. 2000).

7.6.2. Evidence for simultaneous dysfunction in frontal cortex and ventral visual stream in patients with recurrent complex visual hallucinations

7.6.2.1. Evidence from functional imaging. There is consistent evidence for activation in ventral visual areas in patients who are hallucinating and some, less consistent, evidence of abnormal frontal and ventral stream activation in patients who are prone to hallucinations.

Wunderlich et al. (2000) reported a case of hallucinations following occipital stroke. Among other areas, dorsolateral frontal and inferior temporal cortices were activated during active hallucinations. Another case reported by Kishi et al. (2000) had occipital cortex hypoactivity. ffytche et al. (1998) showed in patients with eye disease that ventral stream activation was a consistent feature of hallucinators, but frontal

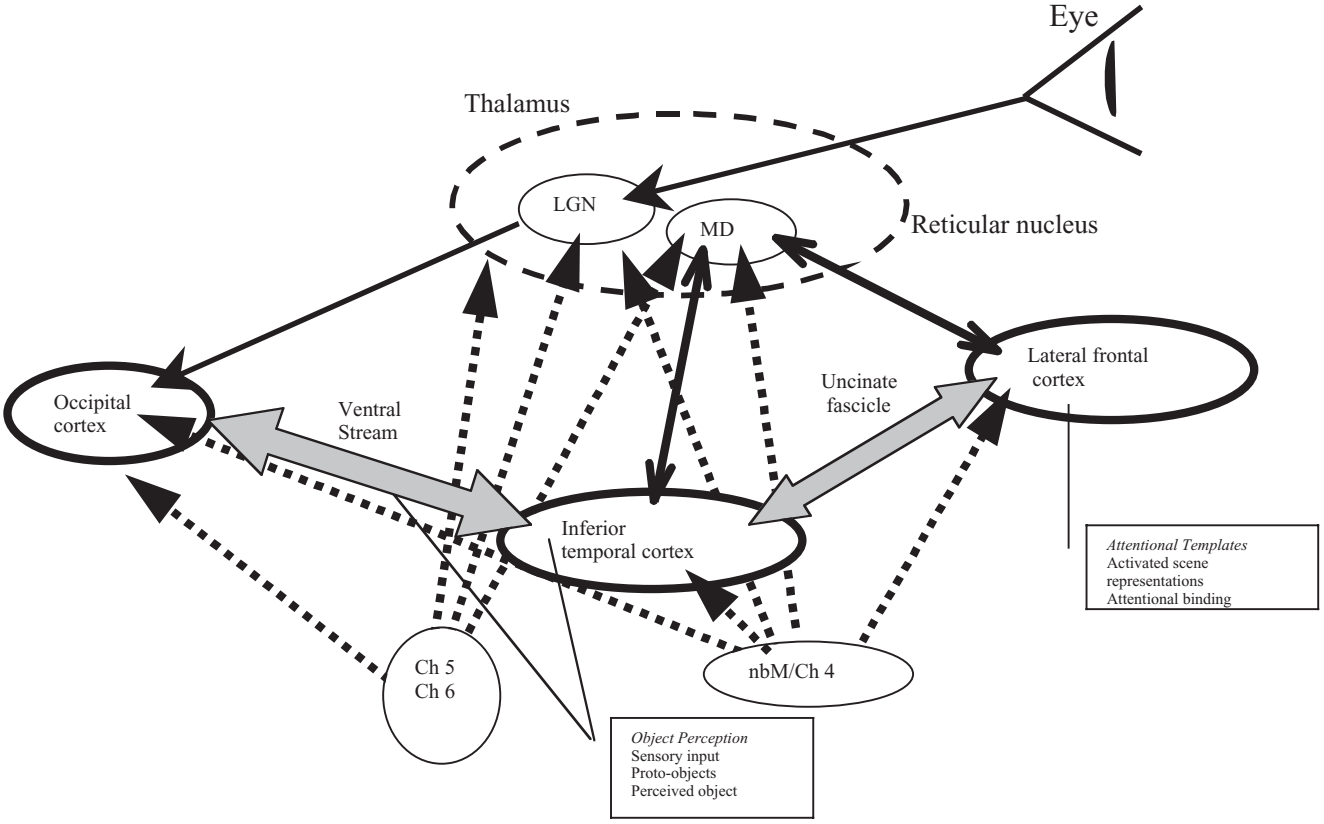

Figure 7. Illustration of the multiple information transfer and regulatory links between cholinergic and thalamic projections and the lateral frontal cortex and ventral stream. Specific thalamic nuclei are intimately involved with visual processing; the lateral geniculate nucleus (LGN) forms the major relay for information from the eye to occipital cortex and thence to the ventral visual stream for object recognition (Sillito & Jones 2002), while the mediodorsal nucleus (MD) maintains active corticothalamocortical loops with the ventral visual stream and, particularly, the frontal cortex (Sherman & Guillery 2002). Basal forebrain cholinergic cells in the nucleus basalis of Meynert (nbM/Ch 4) project to both frontal cortex and the ventral visual stream as well as directly to thalamic nuclei including the reticular, lateral geniculate, and mediodorsal nuclei (Mesulam 1995). Basal forebrain projections to the thalamic reticular formation have an additional regulating role on the transfer of corticothalamocortical information (Guillery et al. 1998). Frontal and inferior temporal cortices are linked by the uncinate fascicle (Ungerleider et al. 1989) and, with other indirect links and nbM cholinergic projections, form a functional visual information processing system (Dudkin et al. 1994; Gaffan et al. 2002; Masuda et al. 1997). Brainstem cholinergic projections from the pedunculopontine nucleus (Ch 5) and laterodorsal tegmental nucleus (Ch 6) also modulate the reticular formation and the mediodorsal nucleus, and, in addition, project to the lateral geniculate and other thalamic nuclei (Mesulam 1995), as well as the occipital cortex (Higo et al. 1996).

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activation was more variable. Silbersweig et al. (1995) showed an association with combined active visual and auditory hallucinations in schizophrenia and increased activity in temporal and frontal cortices, among others. Imamura et al. (1999) showed an association with reduced ventral stream activation and relatively preserved temperoparietal activation in patients with dementia with Lewy bodies who were prone to hallucinations. Okada et al. (1999) showed that in Parkinson's disease, propensity to medication-induced hallucinations was associated with lower resting activation in left temporal and temporo-occipital areas, and, less reliably, right temporal and temporo-occipital areas. Adachi et al. (2000) demonstrated hyperperfusion in the lateral temporal cortex, striatum, and thalamus in hallucinating patients with Charles Bonnet syndrome. Howard et al. (1997) demonstrated that, in dementia with Lewy bodies, active hallucinations lead to a decrease in the responsiveness of striate cortex, suggesting a route for synergy in that hallucinations may in themselves reduce visual function.

In the dreaming state, there are changes in both frontal and inferior temporal cortices (reviewed in Braun et al. 1998; Schwartz & Maquet 2002), among others. However, in dreaming, there is underactivity of frontal cortex, suggesting a lack of attentional and scene-based influences. This may account for the different phenomenology of dreaming and argues further against dream intrusion as an explanation for RCVH.

7.6.2.2. Distribution of pathology in patients with high levels of recurrent complex visual hallucinations. With respect to cholinergic neuropathology, it has consistently been observed that there is a more extensive neocortical cholinergic deficit in dementia with Lewy bodies than in Alzheimer's disease (Perry et al. 1993; Tiraboschi et al. 2000; 2002). This raises the question of whether the higher prevalence of RCVH in dementia with Lewy bodies is related to more extensive cholinergic pathology, consistent with the psychopharmacological evidence reviewed in section 3.2. Based on neurochemical findings in autopsy brain tissue from prospectively assessed cohorts of patients with dementia with Lewy bodies, lower levels of choline acetyltransferase and of the nicotinic receptor subtype α7 are associated with visual hallucinations (Ballard et al. 2000; Court et al. 2001). No such relationships have been established for dopaminergic parameters in the cortex (Piggott et al., submitted), nor for cholinergic activities in the thalamus (Ziabreva et al., in preparation). Furthermore, extensive loss of cholinergic innervation of the thalamus in progressive supranuclear palsy (Javoy-Agid 1994; Kish et al. 1985; Shinotoh et al. 1999) as a result of brainstem cholinergic cell loss is not associated with high rates of hallucinations.

There is a striking relationship between levels of choline acetyltransferase in lateral frontal and temporal cortical areas and rates of visual hallucinations within the major dementing disorders (Fig. 8). In contrast, there is no such relationship with levels in the hippocampus, consistent with the lack of a relationship between verbal memory measures and RCVH (see Fig. 4 legend). This would suggest that localised rather than generalised cerebral dysfunction is critical. In vascular dementia, the relatively high prevalence of RCVH is not paralleled by particularly severe cholinergic deficits. Although hallucinations are rare in stroke, Rabins et al. (1991) showed a combination of intrinsic frontal and ventral stream pathology in hallucinators. This suggests that hallucinations in vascular dementia, and perhaps other disorders (e.g., in dementia with Lewy bodies; see Harding et al. 2002), may result from a combination of cholinergic and other pathologies.

Direct or indirect cholinergic modulation of the neocortical areas implicated in our model can also account for the

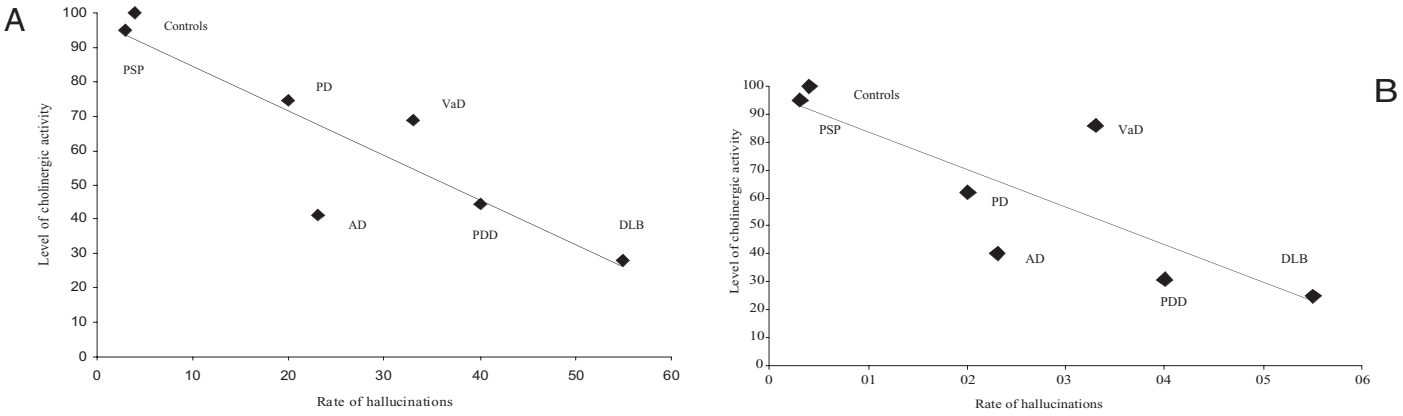

Figure 8. Relationship between cholinergic function and rates of visual hallucinations in dementing and neurodegenerative illnesses in (**A**) inferior temporal cortex (Brodmann Area 20), $r^2 = 0.78$, $p < 0.01$ and (**B**) lateral frontal cortex (Brodmann area 9), $r^2 = 0.65$, $p < 0.05$. Rates of visual hallucinations are taken from Figure 1. Cholinergic function is an averaged percentage of choline acetyltransferase activity of control values. Sources: progressive supranuclear palsy (PSP) (Javoy-Agid 1994; Kish et al. 1985; Shinotoh et al. 1999); Parkinson's disease without dementia (PD) (Perry et al. 1985; Ruberg et al. 1990); Alzheimer's disease (AD) (Bierer et al. 1995; Perry et al. 1977; 1985; 1990; Shaibani & Sabbagh 1998; Tiraboschi et al. 2000; 2002); Parkinson's disease with dementia (PDD) (Perry et al. 1985; Ruberg et al. 1990); dementia with Lewy bodies (DLB) (Perry et al. 1990; Ruberg et al. 1982; Tiraboschi et al. 2002); vascular dementia (VaD) (Perry et al. 1977; Reikkinen et al. 1987; Sakurada et al. 1990; Wallin et al. 1989). Cholinergic function in the hippocampus is not reliably associated with rates of visual hallucinations $r^2 = 0.46$, $p > 0.05$. Sources: AD (Beal et al. 1988; Ikeda et al. 1991; Kuhl et al. 1996; Perry et al. 1977; 1986; 1987; 1992; Sakurada et al. 1990; Smith et al. 1988; Tiraboschi et al. 2000); VaD (Perry et al. 1977; Sakurada et al. 1990); PD (Kuhl et al. 1996; Perry et al. 1986; 1987; Smith et al. 1988); PDD (Beal et al. 1988; Kuhl et al. 1996; Mattila et al. 2001; Perry et al. 1986; 1987; Smith et al. 1988); DLB (Tiraboschi et al. 2000).

induction of visual hallucinations by pharmacologically induced decreases in cholinergic function and their treatment by drugs that counter reduced function (sect. 3.2).

In the context of the PAD model, cholinergic dysfunction in these cortical areas induced by intrinsic anticholinergic factors in delirium could account for RCVH in this disorder. The reduction in function in both brainstem and basal forebrain cholinergic projections as a concomitant of slow-wave sleep (Jones 1993; 2003; Szymusiak et al. 2000; Vazquez & Baghdoyan 2001) may provide a physiological explanation of hypnopompic and hypnagogic hallucinations, with cholinergic hypoactivity occurring on the edges of sleep and loss of consciousness. As hypnagogic/hypnopompic hallucinations (independent of narcolepsy) have been identified as one of the commonest types of RCVH in the population as a whole (Fig. 1), it is clear that understanding the basis of these phenomena would provide insights into RCVH in disease. In narcolepsy, the major deficit of hypocretins (orexins; reviewed in Taheri et al. 2002) that, inter alia, stimulate basal forebrain cholinergic neurons (Eggermann et al. 2001), indicates that RCVH may arise in this disorder as a result of indirect dysfunction of this cholinergic pathway. Although associations between sleep disorder and hallucinations have frequently led to the implication of brainstem cholinergic mechanisms in hallucinations, it is equally plausible that the link between these two phenomena is pathology of the basal forebrain cholinergic system, which plays as important a role in transitions from wakefulness to slow-wave sleep or from non-REM to REM sleep. The hypothesis that hallucinations relate to REM sleep is not consistent with the evidence summarized earlier that hallucinations are associated with decreased cholinergic activity in the cortex, since REM sleep is associated with activity of both brainstem and basal forebrain pathways (in the latter, activity is even higher during REM than during waking; see Vazquez & Baghdoyan 2001).

Eye disease and schizophrenia pose greater challenges to our model, given the lack of established cerebral pathologies in these disorders. Eye disease will clearly result in impaired function in the ventral visual stream, whereas the relationship with cognitive impairment leaves open the question of disruption in frontal attentional function. Despite established neuropsychological impairments (sect. 7.2.1), pathological findings in schizophrenia are highly variable. Recent evidence for thalamic pathology (Jones 1997), together with known corticothalamocortical loops to frontal and ventral steam cortex, suggests one possible biological mechanism (Behrendt & Young 2004). Additional evidence of possible neocortical cholinergic dysfunction is that anticholinergic drugs impair prepulse inhibition of the startle response in schizophrenia (Kumari et al. 2003). Reduced muscarinic receptors have been detected in the cortex and thalamus in unmedicated schizophrenic patients (Raedler et al. 2003), confirming previous autopsy based findings (German et al. 1999; Karson et al. 1993; Powchik et al. 1998). Sherr et al. (2002) have demonstrated that nicotine improves eye tracking in schizophrenic patients, consistent with the long-standing implication of nicotinic receptors in this disease. Very recent reports (Minzenberg et al. 2004) draw attention to the role of the anticholinergic side effects of antipsychotic medication in schizophrenia in inducing cognitive impairment. This suggests a further method by which cholinergic function in schizophrenia may be disturbed.

The clear-cut thalamic dysfunction in deep brain stimulation, thalamic hallucinosis, and fatal familial insomnia can, in contrast, be incorporated in the PAD model, given the strong indirect regulatory pathways via the thalamus to our cortical areas of interest. Unlike other authors, however (Behrendt & Young 2004; Manford & Andermann 1998), we do not assign a central role to thalamic dysfunction in the majority of hallucinations, suggesting instead that this is only one of a number of causative factors.

8. Predictions from the PAD model

As with any multifactor model, falsification can be a challenge. The key concept in PAD is that a hallucination occurs when an incorrect proto-object takes the place of a correct proto-object. We would therefore say that it could be falsified if this were shown not to be so, that is, if an active hallucination could coexist with active perception of a correct image. This might be tested by, for example, combining perceptual tasks with imaging of visual cortex during and outside active hallucinations. Beyond this, we believe that the constraints that the PAD model suggests within visual processing can be tested at several levels.

The PAD model predicts that RCVH will be accompanied by psychological evidence of impaired attention and object perception, resulting in poor scene perception, and by imaging and pathological evidence of frontal and ventral stream dysfunction. The relationships that we have identified among hallucinations, cognitive function, and pathology by averaging disparate data need to be directly tested across at least the major conditions associated with RCVH – dementia, delirium, eye disease, schizophrenia, and the sleep–wake cycle. We would suggest that isolated lesions or impairments only rarely produce RCVH, although other forms of hallucinations or transitory hallucinations may occur. Comparisons across patient groups would allow the necessity for combined impairments to be examined. Thus, we would predict that the 10–20% of blind people who have RCVH also have attentional impairments and pathology that lead to impairments in frontal function.

Beyond these direct tests of existing indirect data, the model makes specific predictions. Thus, scopolamine challenge in normal individuals will induce the same attentional and visual perceptual impairments as seen in patients who hallucinate. The threshold for inducing these will be lower in patient groups prone to hallucinations. Cholinesterase inhibitors will have the opposite effects to those of antimuscarinic drugs. It also suggests that visual hallucinations in schizophrenia will correlate with the antimuscarinic effects of prescribed neuroleptics.

Manipulating the dopaminergic or other systems could assess the specificity of cholinergic dysfunction. We would predict this would only induce visual hallucinations in the context of pre-existing cholinergic dysfunction. Combination of these experiments with in vivo imaging of cholinergic and dopaminergic function in the ventral stream, frontal cortex, and areas thought not to be relevant, would further develop the model. We would predict that neuroimaging of dopaminergic indices such as FPCIT (the dopamine transporter) or D1/D2 receptors will show a weaker relationship with RCVH than would imaging of cholinergic dysfunction by, for example, IBVM.

The model would predict that individuals susceptible to

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hypnagogia or hypnopompia have lower cortical cholinergic activity than those unaffected, and tend towards poorer attentional and perceptual performance, particularly when fatigued.

The relationship between scene perception and hallucinations can be investigated. For example, if hallucinatory scene representations are significant, we would predict an interaction between the frequency of repetition of specific images and the range of locations in which they occur – fewer images should be associated with fewer locations. Our suggestion of relative preservation of scene representations in the context of poor visual attention and perception can be assessed across patient and other groups by, for example, investigating change blindness. We predict that hallucinations should be more closely related to attentional and perceptual impairments than to problems in scene representations per se. Hence, change blindness should be relatively preserved. As the properties of proto-objects are defined, we would suggest that hallucinations should map onto these. The relationship we suggest between distorted and holistic perceptions can be tested.

The PAD model also accounts for existing effective treatments and predicts a range of new possibilities. For example, interventions that improve either attentional or perceptual function should reduce the incidence of RCVH. Thus, on the perceptual side, treatment of impaired vision reduces RCVH (Eperjesi & Akbarali 2004; Menon et al. 2003), as should bright lights or removing the cues that trigger the hallucinatory template by changing the environment (Diederich et al. 2003). Pharmacological improvement of alertness (Wesnes et al. 2001) is effective, as should be modifying the hallucinatory scene representation by associating another image with the environment. Attending to a correct image, for example, a photograph of a hallucinated person, should extinguish the hallucination.

9. Conclusions

We have combined and developed earlier models to account for why some people have recurrent visual hallucinations of a particular character, by relating hallucinations to a specific combination of cognitive impairments and particular patterns of brain dysfunction. At present, we have neuropsychological evidence in about a third of cases of RCVH (those in dementia and neurodegenerative disease, and to a lesser extent delirium, and schizophrenia), with evidence of regional cholinergic underactivity in about three-quarters (dementia and neurodegenerative disease, delirium, and hypnagogic and hypnopompic hallucinations). We look forward to the gathering of further evidence to test PAD and other models of hallucinations.

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NOTES

1. The term *Charles Bonnet syndrome* has been variously used to describe isolated complex visual hallucinations and visual hallucinations accompanied by a range of other phenomena (Menon et al. 2003). Because of this range of uses and because there is no evidence that either definition describes a different subjective experience, we will not use it ourselves.

2. We use the term *object perception* in this context to include not only the perception of inanimate and animate objects but also people, faces, and animals.

Open Peer Commentary

Common or distinct deficits for auditory and visual hallucinations?

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Abstract: The dual-deficit model of visual hallucinations (Collerton et al. target article) is compared with the dual-deficit model of auditory hallucinations (Waters et al., in press). Differences in cognitive mechanisms described may be superficial. Similarities between these models may provide the basis for a general model of complex hallucinations extended across disorders and modalities, involving shared (overlapping) cognitive processes.

The Perception and Attention Deficit (PAD) model of Collerton et al. proposes that a combination of deficits in attentional binding and object perception is essential to the occurrence of recurrent complex visual hallucinations (RCVH). We recently described a model of auditory hallucinations (AH) based on a different combination of deficits, specifically, deficits in intentional inhibition and context binding (Badcock et al. 2005; Waters et al., in press). Our model, herein designated the HEAR model (Hallucinatory Experience of Auditory Representations), was developed and tested in patients with schizophrenia and has not been explicitly applied to other disorders or modalities. Aside from the obvious focus on hallucinations in different sensory modalities, these two models also appear to focus on substantially different cognitive processing abnormalities. However, our commentary draws out similarities between the two models, as this may highlight fundamental constraints that produce hallucinations across all modalities and disorders. Overlapping cognitive mechanisms seem likely, for, as Collerton et al. note, individuals with RCVH often experience hallucinations in other sensory modalities.

Accounting for the wide phenomenological variation of hallucinations is a challenge noted by both Collerton et al. in the target article and Waters et al. (in press). According to the HEAR model, AH in schizophrenia arise at least in part from the intrusion of representations in memory for which specific contextual details have been lost. Consistent with this proposal, Waters et al. (2004) showed that patients with schizophrenia exhibit a more fragmentary recollection of contextual details. The key features of AH (including the compelling sense of reality and omnipotence, involuntariness, non-self-attribution, richness of voice features, and non-vocal experiences) can be accounted for by this subtle interplay between inhibition and memory (Badcock et al. 2005; Waters et al., in press).