stage, and still only at a whole organ level, significantly limiting the refinement of treatment options.

Two kinds of "memory images": Experimental models for hallucinations?

David Ingle

39 Pratt Street, Framingham, MA 01702. **lake@gis.net**

Abstract: Collerton et al. postulate that in a variety of different clinical conditions, hallucinations are derived from object schema lodged in long-term memory. I review two new experiments in which *memory images* can be easily triggered in neurologically intact subjects. These examples of making visible items in memory may provide experimental models for genesis of hallucinations.

Collerton et al. have abstracted from a variety of clinical entities some common traits of hallucinations and have proposed a plausible theoretical framework to account for the circumstances in which these images most often arise. Yet, at the core of their model, the location and physiological nature of the *schematic images* that feed hallucinations remain uncertain.

Are hallucinations akin to the images evoked by electrical stimulation of sites in the temporal lobe (Penfield & Perot 1963)? Or are they derived from more widely distributed networks, including the prefrontal cortex? Discovering how those visual images arise from memory is especially difficult because hallucinations arise unpredictably. Perhaps fMRI or pharmacological analyses of hallucinations would be advanced by studying analogous phenomena in a reliable and safely evoked manner in a laboratory setting. I review here two novel "memory image" phenomena, which might provide useful models for hallucinogenesis.

About 30 years ago I experienced remarkable intrusions of well-formed images at bedtime: the vivid replay of neuron waveforms that I had seen during hours of microelectrode recording earlier that day. Recently, I asked several visual scientists for such anecdotes and netted six recollections similar to my own. Three persons recalled seeing at night sharp images of patterns on computer screens, used earlier that day for psychophysical tests of experimental subjects. One man, driving home in the early morning, nearly swerved his car to avoid colliding with such an apparition. Naturalistic phenomena also appeared. One man, who had spent the afternoon picking avocados, was treated to an array of green blobs at night. Another saw images of swimming fish after a sporting day, and another recalled images of tree branches picked up while helping his tree-surgeon father.

This last individual is now a neuroanatomist and sometimes sees dendritic trees at bedtime. I lately discovered that very similar anecdotes were recounted by Hanawalt (1954), but the phenomenon appears not to have been systematically studied until recently. These recurring images appear similar to the dream intrusions studied by Stickgold et al. (2000) in volunteers who played a video game for several hours and witnessed the same specific images recurring at night. Another experiment form that lab (Merabet et al. 2004) may provide a safe method of increasing receptivity to those recurring images, as the blindfolding of volunteers for only 48 hours led to a high incidence of hypnagogic imagery.

Next, I present data from my own experiments on a rare visual phenomenon as an experimental analogue to the proto-objects postulated by Collerton et al. to be the source of hallucinated forms. About 1% of the academic population may experience *visual persistences* (VPs): vivid positive afterimages of single objects lasting for 15 to 30 seconds after brief fixation and eye closure (Ingle 2005). Although VPs are formed from just-seen objects or drawings and are not derived from long-term memories, new unpublished experiments reveal that certain VPs can reliably trigger *memory images* (MIs). This happened routinely when each of 5 subjects (including myself) formed a VP of an uppercase letter rotated 45 degrees from the vertical. Within 2 or 3 seconds, the VP of the sideways letter rights itself. One does not see the letter rotate, but the upright orientation suddenly replaces the first image. This intrusion from memory of the "canonical" orientation occurs as well with numerals and small faces (photos or schematic drawings).

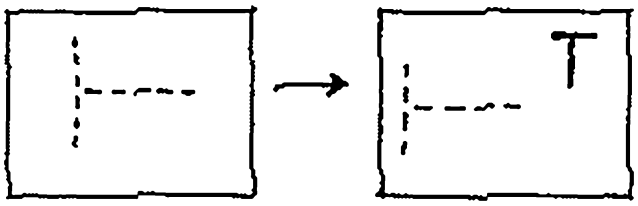

Figure 1 (Ingle). Fixation of a dashed sideward *T* leads to a *visual persistence* (VP) of the unfamiliar pattern. Within 2 or 3 seconds, a *memory image* (MI) of an upright *T* appears on the same index card.

A second example of substitution of an MI for a VP occurs when sideways letters or faces are used to create VPs. After the brief delay, the subject sees two images: the same sideways VP plus the upright MI. Two persons, tested with letters, saw the upright MI overlap with the original VP, whereas three others saw the MI set just to the right of the original VP (Fig. 1). We then found that these MIs are not all simply rotated versions of the VP. First, when the letter (e.g., a sideways *T*) is made of dashed lines, the upright T is seen with solid lines. Second, when the sideways letter is of a less familiar color (purple or yellow-green) the upright letter appears black or grayish. Yet, a familiar ink color (red) is duplicated in the upright MI. These phenomena invite further experiments to determine how much viewing of a given color, line-texture, or font may be necessary for that feature to appear in the MI.

Since the specialization of the fusiform region of temporal cortex for upright faces is now established (Yovel & Kanwisher 2004), I suggest than an analogous specialized representation for upright letters exists for humans (who read regularly) and that this representation readily intrudes upon the VP representation derived from the tilted letter. Although fMRI experiments have found some degree of localization for activations by single letters (e.g., Joseph et al. 2003), our experiments suggest that even better localization might be found by comparing responses of upright to rotated letters. As reliable as letters, numerals, and faces have been in triggering MIs, we have yet to see such effects using tilted or rotated VPs of line drawings of common objects such as fish, cars, bottles, cups, or horses. It seems likely that for these items there are not enough neurons dedicated to the identification of their canonical orientations.

Monoamines in RCVH: Implications from sleep, neurophysiologic, and clinical research

Roumen Kirov

Laboratory of Cognitive Neurodynamics, Institute of Physiology, Bulgarian Academy of Sciences, Sofia, 1113, Bulgaria. **ru@bio.bas.bg**
http://www. bio.bas.bg/~cneurodyn/

Abstract: The role of brain monoamines may be important for the neurobiology of the alterations of visual alertness in recurrent complex visual hallucinations (RCVH). This is evidenced by sleep research, neurophysiologic, and clinical data. Hence, the mechanisms of RCVH may not be simply explained by acetylcholine underactivity only.

The novel Perception and Attention Deficit (PAD) model for recurrent complex visual hallucinations (RCVH), proposed by Collerton et al. in the target article, examines a large body of data

https://doi.org/10.1017/S0140525X05330135 Published online by Cambridge University Press

concerning the occurrence of visual hallucinations in both non-pathological conditions and a range of psychiatric and neurodegenerative disorders. By combining and developing previous models of visual alertness and its alterations, the PAD model gives an advantageous framework for understanding not only the nature of RCVH, but also the processes underpinning visual consciousness. However, in its attempt to provide a unique schema for RCVH in normal and pathological conditions, the PAD model may meet several limitations.

Most of these limitations come from research on the neurobiological mechanisms of the highly varying conscious states across the sleep-wake cycle. In particular, the transition from wake to sleep, when hypnagogic hallucinations normally occur, is basically characterized by a lowering of noradrenergic and serotonergic influences to the cortex rather than only by an acetylcholine underactivity, as Collerton et al. propose. Furthermore, during the transition from sleep to wake, when hypnopompic hallucinations are most frequent, there is a substantial enhancement of the activity of each of the noradrenaline, serotonin, and acetylcholine neurotransmitter systems (Gottesmann 1999; 2004a; Hobson et al. 1975; 2000; Pace-Schott & Hobson 2002). The occurrence of visual hallucinatory-like experiences across sleep stages is most frequently observed during rapid-eye-movement sleep (Fosse et al. 2001; 2004; Hobson et al. 2000), and this sleep stage is characterized by excessive acetylcholine overactivity (Gottesmann 1999; Hobson et al. 1975; Pace-Schott & Hobson 2002). Therefore, RCVH that are normally experienced at the borders of sleep may not be simply explained by acetylcholine underactivity only, as stated by Collerton et al. Rather, the role of either monoamines or monoamine-acetylcholine ratio in these types of RCVH is to be considered. Because the hypnagogic and hypnopompic are the most common visual hallucinations in non-pathological conditions, sleep research data and the neurochemical mechanisms of sleep-wake cycling may certainly be accounted for in explaining RCVH in psychiatric and neurodegenerative disorders.

Furthermore, Collerton et al. suggest that the attention deficit is an important contributing factor for RCVH, with the acetylcholine underactivity being the main neurochemical mechanism. However, many experimental (Aalto et al. 2005; Gao & Goldman-Rakic 2003; Nieoullon 2002; O'Donnell 2003) and clinical data concerning attention-deficit/hyperactivity disorder (Castellanos & Tannock 2002; Swanson et al. 1998) strongly point to the critical role of brain dopamine in the processes of attention. Also, Parkinson's disease (PD), where RCVH are frequently observed (Burn & Troster 2004; Poewe 2003), is caused by degeneration of dopaminergic neurons (Blandini et al. 2000; Eriksen et al. 2005; Fedorow et al. 2005; Montague et al. 2004; Nieoullon 2002). Moreover, there are clinical data documenting that the visual hallucinations in PD can be induced by the dopaminergic therapy (Burn & Troster 2004; Goetz et al. 2001b). Dopamine dysfunction is also generally recognized to underpin the phenomenology of schizophrenia (Hirvonen et al. 2005; Montague et al. 2004; Winterer & Weinberger 2004), which, as mentioned by Collerton et al., is one of the conditions associated with RCVH. Dopamine has an important role in controlling signal-to-noise ratio and top-down processes (Aalto et al. 2005; Gao & Goldman-Rakic 2003; Montague et al. 2004; O'Donnell 2003; Winterer & Weinberger 2004), both suggested in the PAD model to be impaired mainly as a result of acetylcholine underactivity. In addition, noradrenaline and serotonin, along with acetylcholine, are also shown to be significantly involved in modulating the signal-to-noise ratio (Gu 2002).

In the PAD model, the authors propose that hypo-functioning of the lateral frontal cortex resulting from a cholinergic deficit is another mechanism involved in RCVH. In this context, it is to be noted that animal-driven (Gao & Goldman-Rakic 2003; Seamans & Yang 2004; Zhou & Hablitz 1999) and human transcranial magnetic stimulation (Moll et al. 2000; 2003) data show that brain dopamine exerts a strong effect on cortical excitability.

In conclusion, the role of brain monoamines, and the role of dopamine in particular, appears very important for understanding the neurobiology of visual alertness and its alterations in normal and pathological conditions. Hence, the nature of RCVH could hardly be explained by acetylcholine underactivity only.

ACKNOWLEDGMENTS

Preparation of this commentary was supported by DFG, Germany (436-BUL-112/35) and the National Council for Scientific Research, Bulgaria (L-1316).

Mental images: Always present, never there

Fred W. Mast

Department of Psychology, University of Zurich, Cognitive Neuroscience, 8032 Zürich, Switzerland. **f.mast@psychologie.unizh.ch**
http://www.psychologie.unizh.ch/cogneusci

Abstract: Recent research on visual mental imagery plays an important role for the study of visual hallucinations. Not only are mental images involved in various cognitive processes, but they also share many processes with visual perception. However, we rarely confuse mental images with percepts, and recent neuroimaging studies shed light on the mechanisms that are differently activated in imagery and perception.

Visual mental images are generated from memory and therefore are of purely cognitive origin. Behavioral (e.g., Mast & Kosslyn 2002) and neuroimaging research (e.g., Ganis et al. 2004) suggests that the mechanisms associated with mental imagery are – at least to some extent – also involved in visual perception, and the functional value of this overlap has been widely discussed (e.g., perceptual anticipation theory; Kosslyn & Thompson 2003). Even though imagery and perception overlap, only rarely do we actually mistake images for percepts (an exception is the Perky-effect). Why is this the case? Despite the fact that images are essentially involved in a variety of cognitive processes, such as object recognition, spatial reasoning, and problem solving, we hardly ever experience mental images as perceptually real. Why are we able to reliably keep apart or separate when images are generated internally and when images are mediated via sensory stimulation? On the one hand, the fact that several mechanisms are shared by imagery and perception makes it even harder to address this question. On the other hand, research on mental imagery can provide helpful guidance on where to look when studying the mechanisms that account for the occurrence of recurrent complex visual hallucinations (RCVH).

Instead of mental imagery, Collerton et al. focus almost exclusively on attention. The question arises whether the mechanisms that underlie attention have enough explanatory value for a better understanding of RCVH. The major problem is that attention itself has no visual quality, even though it is often involved in visual cognition and visual perception. Mental images are not only phenomenologically related to RCVH, but they also share several common visual properties, which reflect the underlying mechanisms. The target article makes no reference to recent research on mental imagery, which renders Collerton et al.'s model of RCVH not only less compelling, but also incomplete. There are at least three separate points that are noteworthy in this context.

First, the spatial properties of RCVH resemble those of mental images. Collerton et al. point out that hallucinations are located in the central part of the visual field and – unlike afterimages – they do not move with eye movements. This description applies just as well to visual mental images. We often need to inspect images in order to retrieve more specific information from them. Neither images nor hallucinations disappear or move when attended to. Attention can be shifted over imagined or hallucinated objects. Thus, mental images and visual hallucinations share widely the same spatial properties.

Second, it has to be noted that the interplay between visual mental imagery and visual perception is an essential component of top-down processing. When objects are seen from a non-canon-