by, perhaps, the dreamer's inability to perceive a virtual environment. Maintenance of a dream environment may rely preferentially upon visuo-spatial processing subserved by these areas (Mesulam 2000). Lateralization of visuo-spatial function may account for the greater likelihood of dream cessation following right versus left inferior parietal damage (Solms 1997). Dependency on fictive vision for dreaming may be analogous to cessation of RCVH with total blindness and their dependence on dorsal stream integrity, as proposed by Collerton et al. However, dream cessation following left parietal damage and non-visual dreaming following bilateral extrastriate damage (Solms 1997) suggest that fictive dream environments can be based, at least in part, upon other modalities.

Dream visions and RCVH occur in globally differing brain states and cannot be equated. For example, whereas cholinergic deficits often underlie RCVH (Collerton et al. target article), REM sleep shows cholinergic activity equal to, or greater than, in waking within cholinergic projection neurons (Dringenberg & Olmstead 2003) and their terminal fields in the thalamus (e.g., Williams et al. 1994), basal forebrain (e.g., Vazquez & Baghdoyan 2001), and cortex (e.g., Marrosu et al. 1995). Nonetheless, comparison of dreaming with waking pathologies can provide fresh insights into the neural bases of both conditions (Pace-Schott 2005; Schwartz & Maquet 2002).

Hallucinating objects versus hallucinating subjects

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Abstract: Collerton et al. propose that one and the same mechanism (PAD) underlies recurrent complex visual hallucinations (RCVH) in various disorders, including schizophrenia, dementia, and eye disease. The present commentary offers an alternative account of RCVH and other recurrent complex hallucinations specific to schizophrenia and related disorders only. The proposed account is consistent with the bias of schizophrenic RCVH contents toward animate, socially active entities.

The variety of sensory hallucinatory phenomena is characterized by a dichotomy that may be easy to notice and hard to understand. Considering the visual modality separately, Collerton et al. in the target article point at a double dissociation of recurrent complex visual hallucinations (RCVH) versus simple hallucinations including dots, lines, flashes, amorphous shapes, and panoramic landscapes. If a measure of visual complexity is indeed the best separator of the two dissociated categories, then all RCVH are likely to originate from one general mechanism that is distinct from mechanisms underlying other types of hallucinations. Following this logic, Collerton et al. introduce PAD as a general model of RCVH applicable to all cases in which RCVH are observed, including dementias, delirium, schizophrenia, eye disease, and others.

On the contrary, it may seem reasonable to account for RCVH in schizophrenia and, for example, in eye disease based on different mechanisms, if, instead of complexity, another cognitive dimension specific to schizophrenia underlies the dichotomy. Indeed, most hallucinations in schizophrenic states involve various forms of agents engaged in social interactions with the subject (Frith et al. 1998; Mellors 1970; Silbersweig et al. 1995). This happens regardless of the perceptual modality. For example, the following types of auditory hallucinations are characteristic of schizophrenia (Cahill & Frith 1996): voices arguing, voices commenting on one's action, audible thoughts (voices repeat verbatim or comment on subject's thoughts), and voices that command the subject. On the other hand, auditory hallucinations after deafness may include noises and melodies along with singing or talking voices that do not engage in social interactions (Hammeke et al. 1983). The situation is similar with RCVH in non-schizophrenic cases reviewed by Collerton et al. (reviewed in support of PAD). These include RCVH in visual impairment cases described by Charles Bonnet: faces that never smile (Santhouse et al. 2000), RCVH induced by electrical stimulation of the brain (Penfield & Perot 1963), experienced after stroke, in Parkinson's disease (Manford & Andermann 1998), caused by drugs (Hoffmann 1983; Huxley 1959), and so forth. Generally, all non-schizophrenic hallucinations lack a certain degree of animacy and interactive social activity that are typical for schizophrenic hallucinations.

Therefore: (1) Of the following two statements, (a) one and the same mechanism is responsible for RCVH and recurrent complex auditory hallucinations in schizophrenia, and (b) one and the same mechanism is responsible for RCVH in schizophrenia, in dementia and in eye disease, (a) appears to be more credible than (b). (2) The mechanism underlying recurrent complex hallucinations in schizophrenia probably has to do with the concepts of agency, animacy, social interactions, and more generally, the self and its representation in the brain.

A theory based on the latter idea (2), and supported by analysis of clinical and introspective data, was recently proposed by Samsonovich and Nadel (2005). According to this theory, under normal conditions, discrete instances of the subject's own self (labeled *I-Now, I-Previous, I-Next*, etc.) and of the self of any currently perceived external subject, together with all subjective experiences attributed to those instances, are represented in working memory as separate units (*mental states*) that are processed in parallel and interact with one another, obeying a set of hardwired rules (*self axioms*). From this point of view, schizophrenia is a condition in which identities and normal relations among mental states determined by self axioms become lost or altered (Samsonovich & Nadel 2005). As a result, malfunctioning mental states become independent agents and start creating new memories (delusions), engage in dialogues (voices), independently perform imagery (thereby producing hallucinations), or take control of actions. From this point of view, the visual appearance of a socially active RCVH is secondary with respect to its simulated subject, which is a malfunctioning mental state.

Alternatively, one may assume that in schizophrenic RCVH the step of creating a theory-of-mind (ToM) representation of an imaginary character (i.e., "hallucinating a subject") is secondary with respect to developing a sensory hallucination of a face, a body or a voice ("hallucinating an object"). In this case, it would be difficult to understand the nature of the bias toward animate, socially active RCVH in schizophrenia: starting from this point of view, one should expect an opposite bias, toward inanimate or socially inert RCVH, given that ToM abilities are specifically impaired in schizophrenia (Corcoran et al. 1995; 1997; Doody et al. 1998; Frith & Corcoran 1996; Langdon et al. 1997; Sarfati & Hardy-Baylé 1999). It is not clear why the well-known ToM deficit that is characteristic of schizophrenia in general should be reversed in hallucinatory cognitive activity, unless an opposite assumption is made: that in schizophrenia and related disorders, hallucinating a subject (i.e., having a "lost" or misattributed mental state in working memory) causally underlies the hallucination of the related object (face, body, voice). Stated differently, both well-known attributes of schizophrenia – the general ToM impairment and ToM-biased hallucinations – may have one and the same common origin: malfunctioning of the system of mental states (Samsonovich & Nadel 2005).

The PAD model of Collerton et al. has at least several problems; however, the present commentary is focused on one of them: PAD does not account for the specificity of contents of RCVH in schizophrenia and in fact suggests an opposite specificity, as explained above. Although the combined attentional and visual perceptual impairments interacting with internal scene representations could in principle result in a particular schizophrenic RCVH, it is not clear from the point of view of Collerton et al. why there should be a bias toward elaboration rather than simplification of agency and social activity of hallucinated entities. The above analysis suggests that the

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self concept (as it is introduced by Samsonovich & Nadel 2005) could be the key to answering this question and understanding the nature of the dichotomy observed among various types of hallucinations. Finally, incorporating the notion of an imaginary self into the notion of a "proto-object" associated with a living entity may help with further improvements of the PAD model.

The role of acetylcholine in hallucinatory perception

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Abstract: This commentary reviews and extends the target article's treatment of the topic of the role of acetylcholine in hallucinatory experience in health and disease. Particular attention is paid to differentiating muscarinic and nicotinic effects in modulating the use of virtual reality mechanisms by the brain. Then, attention is drawn to the similarities between these aspects of brain function and certain aspects of television digital compression technology.

In the target article, Collerton et al. recognize that normal perception is an amalgam of "down-up" information (*exact inference model* or *I* program) derived from the retinal input (that reports what really is out there) with an "up-down" contribution from stored visual memories (*naïve inference model* or *P* program) as a form of virtual reality (that reports what the brain computes should most probably be out there). An imbalance between these two is associated with repetitive complex hallucinations. The authors then mention the computational model of Yu and Dayan (2002), which modulates this balance. Collerton et al. put this as follows: "Inhibition of cholinergic input gives a greater chance of incorrect pattern matching . . . and allows the intrusion of an incorrect representation" (sect. 7.4.2, para. 2). They suggest that such hallucinations are associated with low cerebral cholinergic activity. As evidence, they mention the hallucinogenic effects of "anticholinergic drugs."

However, the authors do not distinguish clearly between the muscarinic and nicotinic effects of acetylcholine in this situation, which is more complex that appears from their account. The Yu and Dayan model actually states that acetylcholine promotes the retinocortical pathway (essential for the *I* program) by a nicotinic postsynaptic stimulation of cells in layer IV of the cortex, whereas it inhibits corticocortical conductance (essential for the *P* program) by a muscarinic activation of inhibitory presynaptic receptors in cortical layers I/II. This cholinergic activity would promote attention to the environment. The hallucinogenic effects of antimuscarinic agents must therefore depend on a double inhibitory effect on the layer I/II muscarinic system.

In contrast, during a saccade, information from the retina is largely suppressed to be replaced by virtual reality constructed by the brain's *P* processes (Kleiser et al. 2004). A saccade is initiated by a nicotinic signal from the pedunculopontine nucleus (PPN) that initiates the motor corollary of a local increase in *I* activity. Yet, the saccade itself is associated with an increase in *P* activity. It is not known how this is effected, but the following is a possible mechanism. The PPN also has a massive glutamatergic projection to the nucleus basalis. The latter contains many large inhibitory GABAergic interneurons, as well as its cholinergic neurons. It is not known to which of these the PPN projects, but if it is to the former, the GABAergic interneurons, this would supply the necessary mechanism. The projection of the PPN to the superior colliculus would initiate the saccade, and then its indirect projection to the visual cortex via the nucleus basalis would diminish cholinergic activity in that location. The projection from the PPN directly to area 17 mentioned by Collerton et al. is, however, not cholinergic but entirely noradrenergic (Higo et al. 1996).

Most brain structures receive their cholinergic input from only one source. Some, however (such as the intralaminar and medial thalamic nuclei), receive their input from two sources. The superior colliculus belongs to the latter class, as it receives a second cholinergic input from the parabigeminal nucleus, which is part of a midbrain circuit that generates target location information (Cui & Malpeli 2003). The input from the PPN goes to the intermediate layer of the superior colliculus, whereas the input from the parabigeminal nucleus goes to its superficial layer. Here it activates excitatory presynaptic nicotinic receptors on glutamatergic terminals of axons from retinal neurons that synapse on inhibitory GABAergic interneurons. Thus, in this location, the action of acetylcholine is to depress the upward flow of collicular activity (Binns & Salt 2000). The significance of this apparently paradoxical effect is obscure. Incidentally, the only part of the brain that receives no external cholinergic input is the striatum. Here, its cholinergic cells are all involved in local circuits.

The fact that cortical *P* activity is enhanced during a saccade leads one to speculate that one function of the saccades that characterize REM sleep may be to promote the REM state, which is composed of pure, free-wheeling *P* activity (dreams), rather than merely to reflect eye movements directed at dream images, as is supposed at present.

As I have pointed out elsewhere (Smythies 2005), there are interesting parallels between the action of acetylcholine in regulating the *P:I* balance in the cortex and certain aspects of television digital compression technology. Television engineers have discovered that sending every detail of the scene to be televised over the TV channels is very efficient but is also very expensive in terms of computational (and hence financial) cost. This corresponds to our *I* program. So the TV engineers have developed a second (*P*) program that supplements and, in places, replaces the *I* program with material that represents the system's estimate of what should most probably be "out there" based on its memory of the previous outcomes of similar situations. This program is inefficient but cheap in computational cost. This process can involve a third program (the "*P* frame") that records only the differences between successive frames. So the art is finding the best balance between the *P* and *I* programs. The brain seems to follow the same logic. In circumstances when nothing much of interest is happening, the brain can coast along with a $P > I$ ratio. Then, if something of interest occurs, a signal is sent to the nucleus basalis and acetylcholine is released at targeted synapses in the cortex in the manner described above so as to promote activity in areas activated by the new stimulus. This involves changing the ratio to $I > P$ locally or globally. At the same time, the PPN sends a cholinergic (nicotinic) signal to the superior colliculus that initiates a saccade directed towards the computed source of the interesting new stimulus. This is possibly followed by a glutaminergic signal from the PPN to inhibitory neurons in the nucleus basalis that orchestrates the increased $P > I$ ratio that accompanies the saccade itself.

Finally, the authors suggest mechanisms how acetylcholine function could be disturbed in schizophrenia, leading to the hallucinations characteristic of the disease. However, the symptoms of schizophrenia, including the hallucinations, are more probably due to the disturbances of synaptic plasticity, the loss of neuropil and cortical connectivity recently discovered (see Smythies [2004] for details).

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