hyperactivity of dopaminergic pathways, or hypofunction of the corticostriatal glutamate pathways, leading to psychosis (see Carlsson et al. 2000). The direct pathway exerts an excitatory influence, and both pathways are controlled by glutamatergic corticostriatal fibers, serving as brakes and accelerators, respectively (see Carlsson et al. 2000).

We studied perception in an animal model using pigeons. Pigeons were trained in a visual discrimination task, in which reward was linked to recognition of shapes, requiring a high level of attention. We stimulated dopamine receptors and blocked *N*-methyl-*D*-aspartic (NMDA) glutamatergic receptors within the ventral striatum, nucleus accumbens septi (Acc), which is classically linked to schizophrenia (Grace 2000; Matthysse 1981), with an aim to produce an homologous "psychotic-like state," with loss of "gestaltic" discrimination function (Gargiulo et al. 1998). Negative findings were seen with apomorphine or lidocaine injections, but a significant and reversible performance disruption to near chance levels was obtained after 7-aminophosphonoheptanoic acid (AP-7) injection into the Acc (Gargiulo et al. 1998), and, after it, with another NMDA blocker (5-aminophosphonoheptanoic acid (AP-5; Acerbo et al. 2002).

In rats, we observed that by injecting AP-7 within the Acc, acquisition, which requires a high level of attention, is disturbed, with no effects on consolidation (Gargiulo et al. 1999; Martinez et al. 2002b). In these experiments, fecal boli were also diminished during retrieval, suggesting a decrease in anxiety levels during acquisition. For this reason we used a specific anxiety test, the Plus Maze, and we observed that AP-7 clearly decreases anxiety levels when injected within the Acc, suggesting a homologous fact to affective flattening observed in schizophrenia (Martinez et al. 2002a). Taking all these findings as a whole, it appears that Acc integrates cognition and affective levels, and a dysfunction in this nucleus could underlie schizophrenic illness, giving a basis to the understanding of positive (cognitive) and negative (affective flattening) symptoms.

Recently, Grace proposed an interesting circuitry aiming to explain several schizophrenic symptoms (Grace 2000). His hypothesis is that schizophrenia is related to a dysfunction in afferent projections, glutamatergic in nature, converging onto the Acc. He suggested that goal-directed motor plans produced by the prefrontal cortex, the contextual constraints specified by the hippocampus, and the affective evaluation provided by the amygdala are all integrated in the Acc. This integration leads to goal-directed behavior bounded by contextual information and emotional significance. Conversely, in schizophrenia this integration is disturbed, and this fact leads to an abnormal affective drive with an inadequate utilization of contextual cues, resulting in impulsive and disorganized behavior (Grace 2000).

According to our experimental findings, a glutamatergic deficiency on Acc afferences could be at the base of schizophrenia symptoms because perceptual disturbances (Gargiulo et al. 1998), acquisition disturbances (Gargiulo et al. 1997; Martínez et al. 2002b), and decrease in affective levels (Martínez et al. 2002a) can be induced by glutamatergic blockade within the Acc in animal models. Our results link the proposed corticostriatal glutamatergic dysfunction with the thalamocortical disturbances underlying the perceptual problems reviewed by B&Y. In the same way, drugs acting on particular glutamate receptors could lead to new treatments for schizophrenia (see Holden 2003b).

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Absorption, hallucinations, and the continuum hypothesis

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Abstract: The target article, in stressing the balance between neurobiological and psychological factors, makes a compelling argument in support of a continuum of perceptual and hallucinatory experience. Nevertheless, two points need to be addressed. First, the authors are probably underestimating the incidence of hallucinations in the normal population. Second, one should consider the role of *absorption* as a predisposing factor for hallucinations.

A very thin line differentiates internally generated imagery from externally induced perception (e.g., Mast et al. 1999; Mertz et al. 2000), and this is constantly challenged when one broaches the topic of hallucinatory experience, which is the focus of this target article. There is considerable evidence supporting a continuum of perceptual and hallucinatory, or imaginal, experience (Glicksohn et al. 1999; Mahowald et al. 1998; Savage 1975; Slade & Bentall 1988), and even if one considers as valid the distinction between a hallucination and a *pseudohallucination* (Bentall 1990; Berrios & Dening 1996), one can still be somewhat deceived "naturally" (Barrett & Etheridge 1992), experimentally (Perky 1910; Persinger et al. 2000), and when under stress (Siegel 1984). In fact, this seems to be a natural consequence of the Gestalt notion of *Prägnanz*, which states that "psychological organization will always be as 'good' as the prevailing conditions allow" (Koffka 1935, p. 110). If either the external conditions change or the internal state of consciousness changes (or both), the resulting perceptual organization will change, as will the experience (Glicksohn 1998). Behrendt & Young (B&Y) are thus quite correct in summarizing that hallucinations are "underconstrained perceptions that arise when the impact of sensory input on activation of thalamocortical circuits and synchronisation of thalamocortical gamma activity is reduced" (target article, Abstract), both because this is in line with what we stated earlier, and because there are other reports in the literature supporting this claim (Crawford et al. 1993b; Rainville et al. 2002). They are also correct in suggesting that "normal perception in wakefulness is fundamentally a state of hallucinations, one however that is constrained by external physical reality" (sect. 1, para. 3), because similar arguments have been repeatedly made in the literature over the past 30 years (Neisser 1976; Shepard 1984; Yates 1985). But, I think that they are wrong in sharply criticizing the perceptual-release theory (originally advanced by West 1962), claiming that this theory does not explain hallucinations unrelated to sensory deprivation (sect. 3.1), on two counts. First, because the field of sensory deprivation has evolved since then, with newer conceptualizations relevant to the release of quasi-hallucinatory imagery (Glicksohn 1991; 1993; Suedfeld 1980; Suedfeld et al. 1994); and second, because the same type of theory underlies other experimental work in this and relevant domains (e.g., Stoyva 1973). In fact, B&Y's own Figure 5 seems, to my mind, to be a nice elaboration of Figure 2 appearing in West's chapter, yet there is no mistaking their contribution here, in their proposal that neurobiological and psychological aspects are both required for understanding the nature of hallucinations. There are, however, two caveats to be dealt with.

My first point is that B&Y, while understandably focusing more on those hallucinations associated with pathology, are probably underestimating the incidence of hallucinations in the normal population, citing a single source indicating an annual incidence of only 4–5% (sect. 4.2). A number of recently published studies (Glicksohn & Barrett 2003; Johns et al. 2002; Ohayon 2000) indicate a much higher incidence. In our own study (Glicksohn & Barrett 2003), employing both the Barrett Hallucination Questionnaire (BHQ; Barrett & Etheridge 1992) and the Launay–Slade

Hallucination Questionnaire (LSHS; Launay & Slade 1981), we reported the degree of endorsement of each item. These ranged from 2% ("hearing a conversation in the rear of the car") to 41% ("hearing noises") for the BHQ, with a mean degree of endorsement of 11.8%; and between 4% ("hearing the voice of God") and 76% ("voices in the head") for the LSHS, with a mean degree of endorsement of 35.7%. These data do not detract from the arguments made in the target article, but they certainly suggest that the phenomena under discussion are, by far, not only associated with pathology.

My second point is that it is of paramount importance to consider the *interaction* of trait and context in determining subjective experience (Glicksohn 1987) in general, and in particular, with respect to hallucinatory experience. I single out the trait of *absorption* (for a review, see Roche & McConkey 1990). In a recent paper, we presented data indicative of a common pseudohallucinatory experiential base, and suggested that absorption can serve as the predisposing factor for hallucinatory experience (Glicksohn & Barrett 2003). Absorption might very well be viewed as a *diathesis* for hallucination (for general discussions, see Butler et al. 1996; Monroe & Simons 1991). B&Y have ignored the role of individual differences in developing their model, and yet some authors consider the role of such individual differences to be critical for testing the validity of any model (Underwood 1975). Let me give two examples from the target article. The authors write that "it is doubtful that thoughts, inner speech, verbal images, or retrieved memories can be transformed into experiences with perceptual qualities just by virtue of their misattribution to an external origin" (sect. 2, para. 4), but this is exactly what individuals scoring high on absorption seem to do (Destun & Kuiper 1999). Second, the authors argue that when sensory constraints are weak, "then attentional mechanisms may become the dominant modulatory influence on thalamocortical self-organization and hallucinations may arise" (sect. 1.3, Fig. 2 caption). Yet, this is exactly what distinguishes between individuals scoring high and low on absorption (Crawford et al. 1993a). B&Y might well consider the implications of such individual differences for their model.

Paradoxical sleep and schizophrenia have the same neurobiological support

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Abstract: During the paradoxical dreaming sleep stage, characterized by hallucinations and delusions, as in schizophrenia, the increased subcortical release of dopamine, the presynaptic inhibition of thalamic relay nuclei, and serotonergic disinhibition are in accordance with the model for the mechanism of hallucination-induction.

Behrendt & Young (B&Y) develop a highly interesting model based on powerful arguments. Indeed, the thalamus is a crucial step for treatment of sensory information. Moreover, the thalamocortical loop is strongly involved in electrophysiological activities concerned with normal consciousness, in that the gamma rhythm, which is impaired in Alzheimer's disease (Llinas & Ribary 1993), is recorded, most often synchronized, at both levels. The assumption that hallucinations are able to occur in the activated brain when the constraint of sensory afferents is decreased is, of course, very attractive for a sleep researcher, particularly when one is involved in the paradoxical dreaming sleep stage (PS). Indeed, there are strong functional analogies between dreaming and schizophrenic mind disturbances (principally hallucinations and delusions, cognitive impairment). First, already-established results show that there is thalamic postsynaptic activation, but presynaptic inhibition, in relay nuclei during the eye movement bursts of PS (Gandolfo et al. 1980; Steriade 1970), which are in strong relation to dreaming activity (Aserinsky & Kleitman 1953; Dement & Kleitman 1957). These data are in accordance with the hypothesis of sensory deafferentation for PS hallucinatory activity. More recently, the gamma rhythm was discovered in animals (see Maloney et al. 1997) and humans (Llinas & Ribary 1993; Ribary et al. 1991). It occurs during waking as well as during PS, but there is a specific difference when compared to waking. In addition to the absence of reset by sensory stimulation during PS (Llinas & Ribary 1993), recalled by the authors in the target article, which confirms the sensory deafferentation during this sleep stage, the synchronization over the cortical areas disappears during this sleep stage (Perez-Garci et al. 2001). This is an indication of disconnectivity of central structures, which are also repeatedly mentioned for schizophrenia (Meyer-Lindenberg et al. 2001; Tononi & Edelman 2000; Young et al. 1998). Finally, blood flow shows two important facts: (1) Although the associative visual cortex is activated during PS, the primary one is deactivated (Braun et al. 1998), which is also in accordance with some visual deafferentation, the main sensory modality concerned with hallucinatory dreaming activity. (2) There is a prefrontal dorsolateral deactivation both during dreaming (Maquet et al. 1996) and in schizophrenia (Weinberger et al. 1986).

Electrophysiological results related to neurochemistry have shown that noradrenergic and serotonergic neurons that innervate the cortex have mainly inhibitory influences (Araneda & Andrade 1991; Krnjevic & Phillis 1963; Manunta & Edeline 1999; Reader et al. 1979), and that these neurons, active during waking, become silent during paradoxical sleep (Hobson et al. 1975; McGinty & Harper 1976), thus inducing cortical disinhibition during PS (Gottesmann 1999; 2000; 2002). It is worth mentioning that clinical results show a deficit of both transmitters in schizophrenia (Linner et al. 2002; Silver et al. 2000). However, there is one monoamine – dopamine – the activity of which persists during PS (Miller et al. 1983; Trulson & Preussler 1984). It was even hypothesized that these neurons could release more dopamine during PS (Gottesmann 2002), because of firing by bursts (Gonon 1988). Indeed, results have already shown a higher variability of neuron firing in tegmental area neurons during PS (Miller et al. 1983), which implies at least some bursts. Finally, the N_{100} component of the test evoked potential in the prepulse inhibition paradigm shows differences during waking in normal subjects and in schizophrenics; in contrast, an identical increase of amplitude appears during REM sleep, which suggests a disinhibition process in both states (Kisley et al. 2003).

The main neurochemical hypothesis concerning schizophrenia disturbances involves an excess of dopamine functioning, as shown by the improvement by dopamine receptor blockers, and a deficit of glutamate, as shown by NMDA antagonists that induce psychotic symptoms (Grace 2000) and, interestingly, vivid dreaming (Reeves et al. 2001). These dysfunctionings could be responsible for the positive symptoms of schizophrenia (hallucinations, delusions), which mainly concern the nucleus accumbens, whereas a deficit of dopamine at the prefrontal cortex level might induce the negative symptoms of this disease: anhedonia, cognitive impairment (Abi-Dargham & Moore 2003). Moreover, hallucinatory activity and loss of reflectiveness are also observed during PS. Therefore, our laboratory studied dopamine and glutamate release in the medial prefrontal cortex and nucleus accumbens of rats by microdialysis and capillary electrophoresis. The results showed a decrease of dopamine during PS in the medial prefrontal cortex when compared to waking (Gottesmann 2004; Léna et al. 2003). This decrease might cause this transmitter to fall outside the limited range of optimal functioning (Abi-Dargham & Moore 2003) and be responsible for the cognitive impairment observed both during dreaming and in schizophrenia. The level of glutamate was unchanged during sleep–waking stages. In contrast, there was a maximal level of dopamine during PS in the nucleus accumbens, a minimal release during slow wave sleep (SWS), and an intermediate level during waking. Moreover,

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