other words, the brain system generating the evoked response is not linearly characterized by the response to a single stimulus: Temporal context affects the evoked response to primary stimulus information. Mismatch negativity (MMN) is another temporal context effect: Auditory cortex responds differently to the same physical stimulus as a function of its frequency or infrequency of occurrence relative to a physically different stimulus. Although both P50 and MMN may be altered in schizophrenia, MMN depends crucially on NMDA-receptors (Javitt et al. 1996), whereas P50 suppression possibly may not (van Berckel et al. 1998).

Phillips & Pflieger (2000) hypothesized that evoked EEG responses, which are phase-locked to the stimulus, reflect RF processing; whereas induced EEG responses, which are event-related but not phase-locked to the stimulus, reflect CF processing. Grounds for thinking that this may approximately hold, are: (a) phase-locking to the stimulus naturally suggests external event-driven processing; and (b) non-phase-locking with respect to the stimulus may reflect ongoing cortical coordinating activity with intrinsic timing. We devised a high-density EEG pilot study (unpublished) that used complex visual contour integration stimuli consisting of many small Gabor patches (Field et al. 1993), as specially modified by George Lovell (see his submitted doctoral thesis [Lovell 2002]). Pairs of stimuli were presented simultaneously to the right and left visual fields. One stimulus consisted of structured sets of Gabor patches with perceived contours embedded in a background of randomly oriented patches. The second stimulus consisted of the same configuration with 40-degree random jittering of patch orientations (which obliterated perceived contours). The subject's task was to detect "structure right" or "structure left." Average reaction times were about 400 msec with nearly 100% accuracy. Between-condition differences for the broadband average event-related potentials (about 275 epochs per condition) were subtle at best for all scalp locations up to about 250 msec. Evoked and induced responses were calculated using the method of complex demodulation for the following symmetric bands: 10 Hz ± 5 Hz, 20 Hz ± 10 Hz, 30 Hz ± 15 Hz, and 40 Hz ± 20 Hz. A nonparametric permutation procedure was used to convert all differences to uncorrected *p*-value waveforms, with low values (close to 0) indicating left>right visual field differences, and high values (close to 1) indicating right>left visual field differences. Significant induced and evoked 40 Hz differences were observed: Right>left at left para-occipital locations at about 32 msec (induced) and 34 msec (evoked), and left>right at right para-occipital locations at about 76 msec (induced) and 58 msec (evoked). Similar induced, but not evoked, 30 Hz response differences were observed. No induced 20 Hz or 10 Hz differences attained significance, nor did the evoked 20 Hz differences. Evoked 10 Hz differences were about 36 msec for right>left (left para-occipital) and about 26 msec for left>right (right para-occipital). Therefore, both induced and evoked differences were found at the expected sides, with generally slower latencies for structure on the left.

By definition, these subtle differences reflect contextual field processing. Because evoked differences sometimes precede induced differences, this single subject pilot study does not support our hypothesis. However, the finding of relatively early 40 Hz band differences may be meaningful in the context of P&S.

ACKNOWLEDGMENTS

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NMDA synapses can bias competition between object representations and mediate attentional selection

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Abstract: Phillips & Silverstein emphasize the gain-control properties of NMDA synapses in cognitive coordination. We endorse their view and suggest that NMDA synapses play a crucial role in biased attentional competition and (visual) working memory. Our simulations show that NMDA synapses can control the storage rate of visual objects. We discuss specific predictions of our model about cognitive effects of NMDA-antagonists and schizophrenia.

Phillips & Silverstein's (P&S's) target article is a major step in the development of a coherent theoretical framework for understanding how spatially distributed brain activity is coordinated or integrated in normal function, and how this coordination may be impaired in schizophrenia. Their perspective reconciles localist and holist approaches to brain function into a dialectic functional scheme, in which invariant local (modular) processing operations or neural representations are flexibly integrated into larger context- or task-dependent processing or representational units.

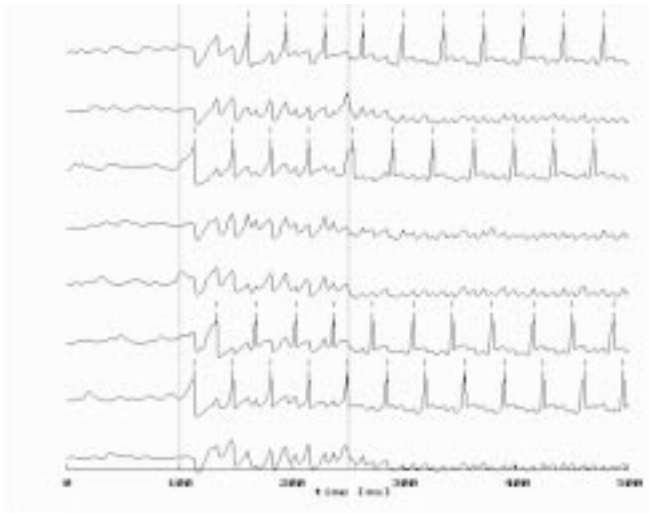
We endorse P&S's view on the crucial role of NMDA synapses in cognitive coordination and control, based on their amplifying voltage-dependent properties. Specifically, the gain-control properties of NMDA synapses on ongoing processing discussed in the target article may be plausibly involved in selective encoding and maintenance of task-relevant information in cortical networks of (visual) working memory.

In our neurocomputational approach to maintenance and control in visual working memory (Raffone & Wolters 2001; Raffone et al. 2001), the neural representations of features and objects are kept active after stimulus-offset by feedback connections from prefrontal cortex to posterior cortical areas. In this model, object features are integrated by synchronizing connections (*within-chunk integration*), and different objects are segregated by fast mutual inhibition (*between-pattern segregation*). The storage capacity reflects the equilibrium point between these two neural representational forces. In a current study (Raffone et al., in preparation), cortical feedback, within-chunk integration, and between-pattern segregation are combined with NMDA synapses. In this commentary we will outline how NMDA synapses can play a crucial role in *biased attentional competition* (Desimone & Duncan 1995) between neural representations of objects, and discuss specific implications and predictions from our model consistent with P&S's general perspective.

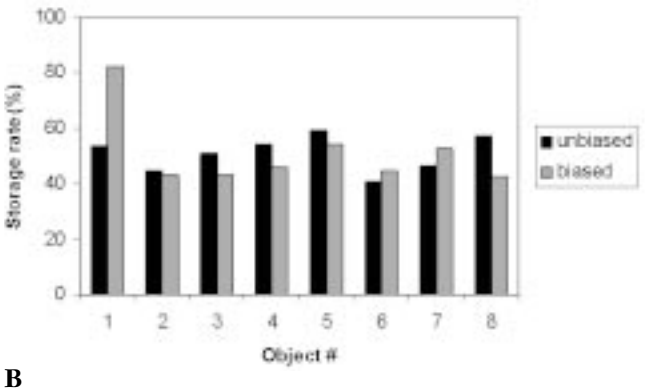
Competition between object representations is a fundamental aspect in many theories of visual attention. For instance, in Bundesen's (1990) Theory of Visual Attention (TVA), the units of visual representation are parallel categorizations of visual elements in limited-capacity visual short-term memory. These categorizations compete in terms of parallel processing speed (affecting the storage probability), which depends on the relative *attentional weight* of visual elements. Theories of attention often refer to the concept of *biased competition* principle between object representations (Desimone & Duncan 1995). According to the biased competition model, the attentional weights (saliency or priority values) of different objects (saliency or priority values) are correlated with selectively biased firing rates of associated competing neural representations in the visual cortex.

It is generally assumed that attentional weights are encoded in terms of firing rate modulation by top-down cortical feedback, plausibly from prefrontal cortex. NMDA synapses, because of their voltage-dependent properties, can implement a gain mechanism in which bottom-up signals are selectively amplified, de-

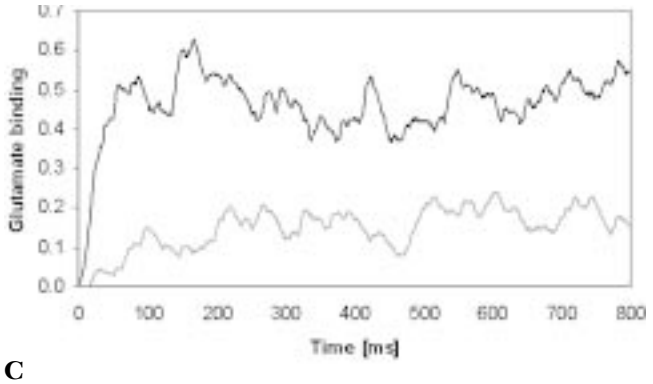
https://doi.org/10.1017/S0140525X03400022 Published online by Cambridge University Press



A



B



C

Figure 1 (Raffone et al.). NMDA-dependent biased competition effects in visual working memory storage. (A) Typical evolution of membrane potentials of eight model neurons from eight parietal assemblies coding for eight different objects (stimulus onset is at 100 msec, and offset at 250 msec; only four objects are maintained after stimulus offset). (B) Percent storage rate of eight objects with (grey bars) and without (black bars) bias toward Object 1, over 200 trials with a storage capacity of about four objects. (C) Glutamate binding at NMDA synapses for attended (black curve) and unattended (grey curve) objects. See text for further explanations.

pending on their top-down saliency. They can, therefore, implement a multiplicative computational scheme in attentional processing, as in Bundesen's (1990) TVA.

We have simulated this NMDA-dependent gain effect in visual working memory storage (Raffone et al., in preparation). In the model, separate objects are encoded by disjoint sets of recurrently-coupled neural assemblies located in the inferotemporal cortex, parietal cortex, and prefrontal cortex. Neural assemblies in parietal cortex receive top-down NMDA signals from *control assemblies* with a differential firing rate located in a prefrontal area.

In the simulation series shown in Figure 1, the cortical network model was presented with displays of eight objects. Given that on average only four objects are stored in terms of reverberations in the absence of any attentional bias (Raffone & Wolters 2001), the storage rate for each object is about 50%. Figure 1A shows the typical evolution of membrane potentials (firing patterns) of eight parietal neurons coding for different objects, with interneuron time-lags reflecting between-pattern segregation. In Figure 1B, the storage rate of eight objects over 200 trials is shown with and without attentional bias toward Object 1. Note the higher storage rate of Object 1 with the amplifying effect of NMDA function (in terms of latent glutamate binding, see Fig. 3 in the target article) added to the parietal assembly coding for it, as compared with the unbiased condition. All the other structural and dynamic parameters are kept constant across the two conditions. Figure 1C shows the evolution of latent NMDA synaptic signals (amount of bound glutamate modeled in terms of a dual exponential with rise time of 5 msec and decay time of 50 msec) to target and distractor assemblies in the biased attentional weight condition.

As shown by our simulations, an important property of NMDA signals is that they are voltage-dependent, and therefore are enabled only in the presence of bottom-up input (sensory evidence). In our model, this dynamic property is also crucial to prevent spurious activation spreading to irrelevant neurons by feedback connections from prefrontal cortex during maintenance. In this case, NMDA signals are generated at the level of recurrent connectivity intrinsic to neural assemblies in posterior areas, and top-down signals from prefrontal cortex selectively act on non-NMDA input-activated assemblies with a sufficient amount of intrinsic glutamate binding. Therefore, reverberations for maintenance only capture input-activated neurons in feature and location dimensions. The absence of NMDA from this circuitry would imply either reduced maintenance capacity or the emergence of hallucinatory neural representations.

If NMDA synaptic systems are impaired in schizophrenia, as suggested by P&S in the target article, and if NMDA synapses play a crucial role in attentional selection and control of storage and maintenance in visual working memory, as suggested by our model, then differences between groups of schizophrenic patients and control groups are predicted in cognitive tasks with interactions between visual working memory and selective attention. Similar functional and pathological principles may be involved in auditory (verbal) working memory and selective attention. Our model also predicts hallucinations as a result of spurious activation spreading from prefrontal cortex to posterior cortical areas under the effect of NMDA-antagonists, and, following P&S, in schizophrenia.

Why do schizophrenic patients hallucinate?

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Abstract: Phillips & Silverstein argue that schizophrenia is a result of a deficit of the contextual coordination of neuronal responses. The authors propose that NMDA-receptors control these modulatory effects. However, hallucinations, which are among the principle symptoms of schizophrenia, imply a flaw in the interactions between neurons that is more fundamental than just a general weakness of contextual modulation.

The target article distinguishes between "primary input" and "contextual input" onto a neuron. Primary input drives the cell and

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