

analyzing the biophysical properties of the TRPM7 conductance by performing patch-clamp studies on fused giant synaptic vesicles. Such studies would also facilitate characterization of the mechanism through which TRPM7 may be activated in the membrane of synaptic vesicles. TRPM7 is a “chanzyme” consisting of fused channel and protein kinase domains (Nadler et al., 2001; Runnels et al., 2001), and while the authors showed that the channel activity is clearly required for neurotransmitter release, we do not know if the protein kinase contributes to TRPM7 function in synaptic vesicles.

Despite questions concerning the exact mechanism through which TRPM7 regulates release of acetylcholine, the current study provides the first demonstration of a role for a Group 1 TRP in an intracellular membrane, as opposed to the plasma membrane. The Group 1 TRPs include TRPs that fall into the five subfamilies (TRPC, TRPV, TRPM, TRPA, and TRPN) that are most related to the original member of the superfamily, *Drosophila* TRP. Members of the distantly related Group 2 TRPs, such as TRPP2 and TRPML1, are known to be present primarily in intracellular compartments, although their precise functions remain elusive. The concept that such TRP channels are waiting in a dormant state to undergo regulated translocation to the plasma membrane almost certainly applies in some cases. Nevertheless, given the findings by Krapivinsky et al., it may turn out that many TRP channels, which are currently considered cation influx channels, have equally important roles in a variety of secretory vesicles and intracellular organelles.

Craig Montell¹

¹Department of Biological Chemistry
The Johns Hopkins University School of Medicine
Baltimore, Maryland 21205

Selected Reading

- Jiang, J., Li, M., and Yue, L. (2005). *J. Gen. Physiol.* 126, 137–150.
- Krapivinsky, G., Mochida, S., Krapivinsky, L., Cibulsky, S.M., and Clapham, D.E. (2006). *Neuron* 52, this issue, 485–496.
- Morenilla-Palao, C., Planells-Cases, R., García-Sanz, N., and Ferrer-Montiel, A. (2004). *J. Biol. Chem.* 279, 25665–25672.
- Munsch, T., Freichel, M., Flockerzi, V., and Pape, H.C. (2003). *Proc. Natl. Acad. Sci. USA* 100, 16065–16070.
- Nadler, M.J., Hermosura, M.C., Inabe, K., Perraud, A.L., Zhu, Q., Stokes, A.J., Kurosaki, T., Kinet, J.P., Penner, R., Scharenberg, A.M., and Fleig, A. (2001). *Nature* 411, 590–595.
- Rahamimoff, R., and Fernandez, J.M. (1997). *Neuron* 18, 17–27.
- Reigada, D., Diez-Pérez, I., Gorostiza, P., Verdaguer, A., Gómez de Aranda, I., Pineda, O., Vilarrasa, J., Marsal, J., Blasi, J., Aleu, J., and Solsona, C. (2003). *Proc. Natl. Acad. Sci. USA* 100, 3485–3490.
- Runnels, L.W., Yue, L., and Clapham, D.E. (2001). *Science* 291, 1043–1047.
- Runnels, L.W., Yue, L., and Clapham, D.E. (2002). *Nat. Cell Biol.* 4, 329–336.
- Singh, B.B., Lockwich, T.P., Bandyopadhyay, B.C., Liu, X., Bollimunta, S., Brazer, S., Combs, C., Das, S., Leenders, A.G., Sheng, Z., et al. (2004). *Mol. Cell* 15, 635–646.

Can One Suppress Subliminal Words?

Subliminal words cause behavioral priming, yet the depth of their processing remains debated. Using transcranial magnetic stimulation (TMS), Nakamura et al. demonstrate in this issue of *Neuron* that this subliminal priming effect can be selectively disrupted. Distinct TMS sites disrupt priming in lexical decision and pronunciations tasks, suggesting that task set influences subliminal processing.

The topic of subliminal images readily evokes an infamous episode of the US presidential campaign where a republican television clip associated Al Gore’s face with the subliminal presentation of the word “rats.” Psychologists have long known that words that are briefly flashed can easily be made invisible by preceding and following them with nonsense shapes that serve as visual masks. The key issue, which has been stimulating intense experimental research since Tony Marcel’s seminal studies in the 1980s, is how deeply are such subliminal words processed. Can they activate orthographic, phonological, or even semantic levels of representation? Which brain areas do they contact? Can the conscious strategies adopted by the subjects shape the path that they take? In this issue of *Neuron*, Nakamura et al. (2006) provide an elegant answer to some of these questions.

The authors asked Japanese subjects to perform either a lexical decision task or a pronunciation task on words and pronounceable nonwords that were presented visually or auditorily. Unbeknownst to the subjects, a subliminal visual word, which could be identical or distinct from the target word, was also presented on each trial. In a first experiment, Nakamura and his colleagues show that this hidden word produces reliable repetition priming effects. In both tasks, subjects responded faster to repeated stimuli than to nonrepeated prime-target pairs. Remarkably, this subliminal priming effect was observed within the visual modality, but also crossmodally (from a visual prime to an auditory target).

In a second experiment, the authors replicated this experiment while single-pulse transcranial magnetic stimulation (TMS) was applied either to a left inferior parietal area previously thought to play a role in grapheme-phoneme conversion or to a left superior temporal area implicated in crossmodal word integration. The original aspect of their study was to examine whether TMS, which was applied just prior to the prime presentation, could suppress subliminal repetition priming. The answer, remarkably, depended on the task. When subjects were consciously engaged in the lexical decision task, TMS of temporal cortex abolished behavioral repetition effects, while parietal TMS left repetition priming intact. Conversely, when subjects were engaged in the pronunciation task, parietal TMS but not temporal TMS suppressed repetition priming. This double dissociation strongly suggests that the very same masked words were processed through distinct neural pathways depending on the task performed. Curiously enough, target-driven response times were not affected by TMS,

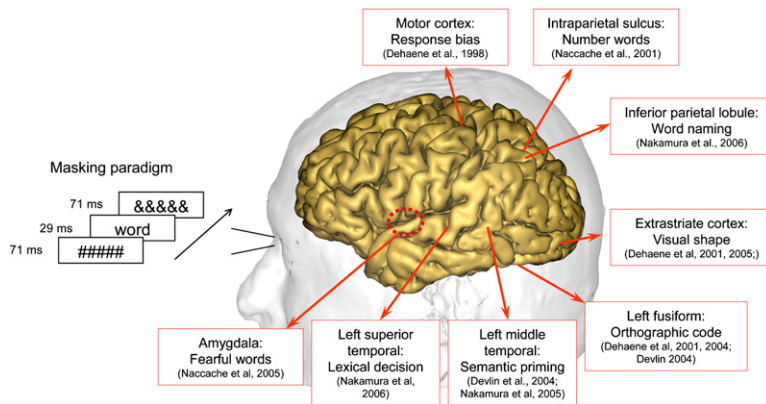


Figure 1. Outline of the Main Regions where Subliminal Masked Words Have Been Found to Cause Activation or Priming (fMRI Repetition Suppression)

The figure also shows the two new regions identified indirectly in the present study as sites where TMS interferes with behavioral subliminal priming (Nakamura et al., 2006).

suggesting that its intensity and timing were carefully adjusted to cause only a transient disruption of prime processing.

The Nakamura et al. study goes beyond previous studies of subliminal priming in several respects. First, it adds to growing evidence that the processing of subliminal words can be very extensive (see Figure 1). Previous research established that hidden primes can cause visual and orthographic priming in extrastriate and fusiform cortices (Dehaene et al., 2001) but also semantic priming in the left middle temporal gyrus (Devlin et al., 2004; Nakamura et al., 2005), as also shown by the N400 component of event-related potentials (Kiefer and Brendel, 2006). Other areas are also activated nonconsciously when the subliminal words belong to a particular semantic category, for instance the amygdala for fearful words (Naccache et al., 2005) or the intraparietal cortex for number words (Naccache and Dehaene, 2001). The present study adds two additional areas to this list of regions capable of subliminal processing: the left superior temporal region and the left inferior parietal lobule. The emerging picture, though still patchy, is consistent with the idea that the entire posterior network of areas involved in reading can be contacted in a feed-forward manner by a subliminal word.

An interesting discovery made by Nakamura et al. is that subliminal priming effects can be crossmodal, from visual primes to auditory targets. A previous study had proposed that crossmodal priming required the primes to be consciously seen (Kouider and Dupoux, 2001). By demonstrating crossmodal priming under conditions where subjects are strictly at chance in a perceptual judgment on the primes, Nakamura et al. clearly show that this is not the case. It may be relevant, however, that Nakamura et al. used a highly regular script, the Japanese kana syllabary, while the majority of previous priming studies were based on alphabetic scripts which are notoriously low in orthographic transparency (English and French). It is possible that the automaticity of spelling-to-sound conversion contributes to the ease with which subliminal crossmodal priming can be observed, a hypothesis that could be tested for instance in Italian or Finnish readers.

In theory, crossmodal priming could have at least two sources: the prime and the target might both contact a shared amodal representation common to written and spoken words, or the prime might be quickly con-

verted by a grapheme-to-phoneme conversion route to a modality-specific region coding for spoken words. Because the present study used only repetition priming, one cannot determine yet which explanation holds, either for superior temporal cortex or for inferior parietal cortex. Determining in what format the words are encoded in those regions would require a new study manipulating specifically the lexical, semantic, and phonological distance between prime and target.

But perhaps the most important implications of the Nakamura et al. study concern our concept of *automaticity*. Many theories of human cognition postulate that nonconscious cognitive processes are automatic and independent of attention. Recently, however, experimental reports using the masked priming paradigm have revealed that subliminal processing is affected by several top-down effects (see Table 1). By showing that repetition priming can be suppressed by applying TMS to distinct locations depending on the task, the present results strongly support this point of view. During the lexical decision task, repetition priming depends primarily on the left superior temporal gyrus, while during the word pronunciation task, it relies mostly on a route passing through the inferior parietal lobule. Those results support the idea that a whole chain of processing defined by the task, once prepared consciously, can be applied to nonconsciously perceived stimuli. Thus, “subliminal” is not synonymous with “automatic” or “task-independent.” Our expectations shape our processing of subliminal stimuli.

It seems appropriate, however, to end with a word of caution concerning the inferences that can be drawn from this TMS study. The two central conclusions of the paper, that the stimulated brain areas are directly involved in subliminal processing of the hidden primes and that their subliminal activation changes with the task, are based on indirect inference. Alternative interpretations of the result therefore remain possible. One possibility is that the task does not really affect subliminal processing—but only the response time measure used to assess it. This proposal would be consistent with Simos et al.’s beautiful demonstration that, for different types of words and pseudowords, naming speed is determined by the onset of activity in distinct brain circuits (Simos et al., 2002). The disappearance of behavioral repetition priming after TMS need not imply that TMS destroys any trace of the prime-induced activation,

Table 1. Top-Down Effects on the Processing of Nonconscious Masked Stimuli

Top-Down Mechanism	Type of Experiment	References	Main Findings
Spatial attention	Behavior in blindsight patient GY and in normal subjects	(Kentridge et al., 1999; Lachter et al., 2004)	Nonconscious stimuli are processed only when presented within the focus of spatial attention
Temporal attention	Behavior and event-related potentials	(Kiefer and Brendel, 2006; Naccache et al., 2002)	Masked word or numbers cause stronger priming when presented within the focus of temporal attention
Task-setting	Behavior and transcranial magnetic stimulation	Present study	Anatomical location of the relevant site of TMS disruption of a masked word depends on the current task
Response instructions	Behavior, ERP and fMRI evidence	(Dehaene et al., 1998; Eimer and Schlaghecken, 1998)	Arbitrary response instructions, learned consciously, are applied to nonconscious stimuli
Stimulus-induced strategy	Behavior	(Greenwald et al., 2003)	The set of conscious targets affects which digits of a nonconscious two-digit number are processed

but merely that it tampers with the normal decision-making process that leads to a fast response time sensitive to priming. Even during the TMS blocks, it is very likely that repetition priming was still present in the left fusiform gyrus, a region associated with orthographic priming. To fully understand which pathways a subliminal stimulus takes, it would therefore seem highly desirable to probe them more directly, for instance by using the same exact tasks and stimuli in an fMRI repetition-suppression design.

A final issue concerns the timescale of such priming effects. If single-pulse TMS were applied to other moments of the prime-target pair, would it be possible to more precisely map the time course of prime processing in different areas? Would the results confirm earlier suspicions that subliminal priming effects are extremely short-lived? Or would it show that, in some areas, masked words are still represented 700 or 800 ms after stimulus onset (Naccache et al., 2005)? While the Nakamura et al. study leaves little doubt that the word “rats” in the anti-Gore campaign was effective in contacting a variety of crossmodal representations of words in the viewers’ brains, gaining a better understanding of the time course of such subliminal activation will be essential in order to evaluate its potential impact on our decisions.

Stanislas Dehaene^{1,2} and Lionel Naccache^{1,3}

¹INSERM, Cognitive Neuroimaging Unit
Service Hospitalier Frédéric Joliot
Orsay
France

²Collège de France
Paris
France

³Hôpital de la Salpêtrière
Clinical Neurophysiology Department
Paris
France

Selected Reading

Dehaene, S., Naccache, L., Le Clec, H.G., Koechlin, E., Mueller, M., Dehaene-Lambertz, G., van de Moortele, P.F., and Le Bihan, D. (1998). *Nature* 395, 597–600.
Dehaene, S., Naccache, L., Cohen, L., Bihan, D.L., Mangin, J.F., Poline, J.B., and Riviere, D. (2001). *Nat. Neurosci.* 4, 752–758.

Devlin, J.T., Jamison, H.L., Matthews, P.M., and Gonnerman, L.M. (2004). *Proc. Natl. Acad. Sci. USA* 101, 14984–14988.
Eimer, M., and Schlaghecken, F. (1998). *J. Exp. Psychol. Hum. Percept. Perform.* 24, 1737–1747.
Greenwald, A.G., Abrams, R.L., Naccache, L., and Dehaene, S. (2003). *J. Exp. Psychol. Learn. Mem. Cogn.* 29, 235–247.
Kentridge, R.W., Heywood, C.A., and Weiskrantz, L. (1999). *Proc. R. Soc. Lond. B. Biol. Sci.* 266, 1805–1811.
Kiefer, M., and Brendel, D. (2006). *J. Cogn. Neurosci.* 18, 184–198.
Kouider, S., and Dupoux, E. (2001). *Cognition* 82, B35–B49.
Lachter, J., Forster, K.I., and Ruthruff, E. (2004). *Psychol. Rev.* 111, 880–913.
Naccache, L., and Dehaene, S. (2001). *Cereb. Cortex* 11, 966–974.
Naccache, L., Blandin, E., and Dehaene, S. (2002). *Psychol. Sci.* 13, 416–424.
Naccache, L., Gaillard, R., Adam, C., Hasboun, D., Clémenceau, S., Baulac, M., Dehaene, S., and Cohen, L. (2005). *Proc. Natl. Acad. Sci. USA* 102, 7713–7717.
Nakamura, K., Dehaene, S., Jobert, A., Le Bihan, D., and Kouider, S. (2005). *J. Cogn. Neurosci.* 17, 954–968.
Nakamura, K., Hara, N., Kouider, S., Takayama, Y., Hanajima, R., Sakai, K., and Ugawa, Y. (2006). *Neuron* 52, this issue, 557–564.
Simos, P.G., Breier, J.I., Fletcher, J.M., Foorman, B.R., Castillo, E.M., and Papanicolaou, A.C. (2002). *Cereb. Cortex* 12, 297–305.

DOI 10.1016/j.neuron.2006.10.018

Kv1.1 Takes a deTOR from the Axon to the Dendrite

In the October 6th issue of *Science*, Raab-Graham et al. described two surprising findings. They discovered that local dendritic translation of Kv1.1 occurs in CA1 dendrites of rat hippocampal slices and in cultured neurons. This local translation is inhibited by NMDA receptor-mediated synaptic signaling acting through the mTOR kinase.

The regulation of dendritic Kv1 channel expression, and ion channel expression in general, has now been greatly expanded by the exciting work of the Jan lab (Raab-Graham et al., 2006). In their recent report in *Science*, Jan and her colleagues found the first evidence for local activity-regulated local translation of Kv1 channels in