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those from alternative nitrogenases. However, the quartet puzzling support and bootstrap values are not high enough to rule out alternative topologies. The maximum-likelihood branch lengths in Fig. 3 suggest that FS406-22 *NifI*₁ and *NifI*₂ are the shortest distance to the internal node that represents the ancestral P_{II} protein. A recent reconstruction of the tree of life with 31 universal gene families supports the hypothesis that the last universal common ancestor lived at high temperatures (29). We propose that among diazotrophic archaea, the nitrogenase from FS406-22 might have retained the most ancient characteristics, possibly derived from a nitrogenase present in the last common ancestor of modern life.

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Materials and Methods

SOM Text

Figs. S1 to S4

Tables S1 to S4

References

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Greater Disruption Due to Failure of Inhibitory Control on an Ambiguous Distractor

Yoshiaki Tsuchida,¹ Yuka Sasaki,^{2,3} Takeo Watanabe^{1*}

Considerable evidence indicates that a stimulus that is subthreshold, and thus consciously invisible, influences brain activity and behavioral performance. However, it is not clear how subthreshold stimuli are processed in the brain. We found that a task-irrelevant subthreshold coherent motion led to a stronger disturbance in task performance than did suprathreshold motion. With the subthreshold motion, activity in the visual cortex measured by functional magnetic resonance imaging was higher, but activity in the lateral prefrontal cortex was lower, than with suprathreshold motion. These results suggest that subthreshold irrelevant signals are not subject to effective inhibitory control.

We experience an overwhelming amount of visual stimuli. However, a great number of the stimuli are not consciously perceived (are invisible) for a number of reasons, including weakness of the stimuli (1, 2), task irrelevance (3, 4), interference by other stimuli (1, 5–10), and combinations of these factors. Nevertheless, an invisible stimulus can influence brain activity and task performance (1, 2, 10–12). One would naturally assume that the degree of an invisible stimulus's influence is generally weaker than that of a visible stimulus.

We conducted a series of psychophysical and functional magnetic resonance imaging (fMRI) experiments. During each trial of experiment 1, 15 participants were presented with a sequence of eight items (two digits and six alphabetic letters) at the center of a computer screen. In the background, a dynamic random-dot (DRD) display with coherently moving dots (signal) and randomly moving dots (noise) (2, 13–15) was presented (Fig. 1). The participants were instructed to focus on and report the two digits. This task is known as the rapid serial visual presentation (RSVP) task. The background DRD display was thus task-irrelevant (16). The ratio of signal dots to the total number of dots (coherence ratio) was varied from trial to trial. A higher motion coherence task-relevant condition strongly activates monkey middle temporal (MT) (17) and human MT+ (18), which are the visual areas that are largely specialized for motion processing. These findings would naturally lead to the prediction

that a higher task-irrelevant motion coherence stimulus would also produce stronger internal signals within the visual system, which either would result in greater disturbance in task performance (2, 19, 20) or would not influence task performance because of attentional filtering or the suppression of, if weak, irrelevant signals (21).

Performance with coherent motion $\geq 20\%$ did not significantly differ from performance with 0% coherent motion (Fig. 2A). This is consistent with the attention-filtering hypothesis (21) in that task-irrelevant motion coherence signals (at least $\geq 20\%$) did not influence task performance. However, at 5% coherence ratio, performance was significantly lower than at 0 and 20% coherence ratios. Immediately after the main condition, we conducted a test to measure motion coherence ratio threshold (16). The participants were instructed to indicate one of the four coherent motion directions used in the main condition in a

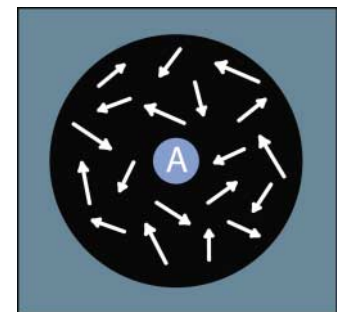


Fig. 1. Stimulus. A sequence of letters and digits was presented in the center while dots moved in the background. The ratio of the number of coherently moving dots to the total number of randomly moving plus coherently moving dots was varied from trial to trial. Arrows represent motion vectors.

¹Department of Psychology, Boston University, 64 Cummings Street, Boston, MA 02215, USA. ²Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA 02129, USA. ³Exploratory Research for Advanced Technology (ERATO) Shimojo Implicit Brain Function Project, California Institute of Technology, Pasadena, CA 91125, USA.

*To whom correspondence should be addressed. E-mail: takeo@bu.edu

DRD display whose coherent motion ratio was varied in seven steps from trial to trial. The result showed that the 5% coherence ratio produced chance-level performance and therefore can be considered to be a subthreshold motion ratio condition (2). Thus, although suprathreshold task-irrelevant signals (e.g., 20%) were successfully filtered out (21), those below but near the chance-level threshold led to disturbance of task performance.

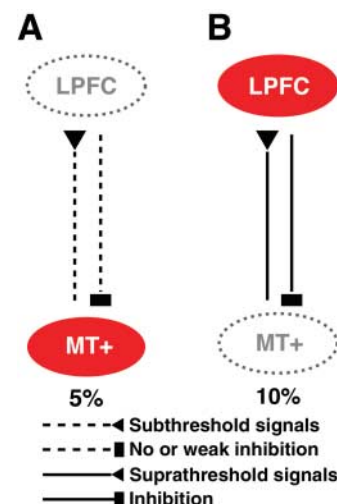
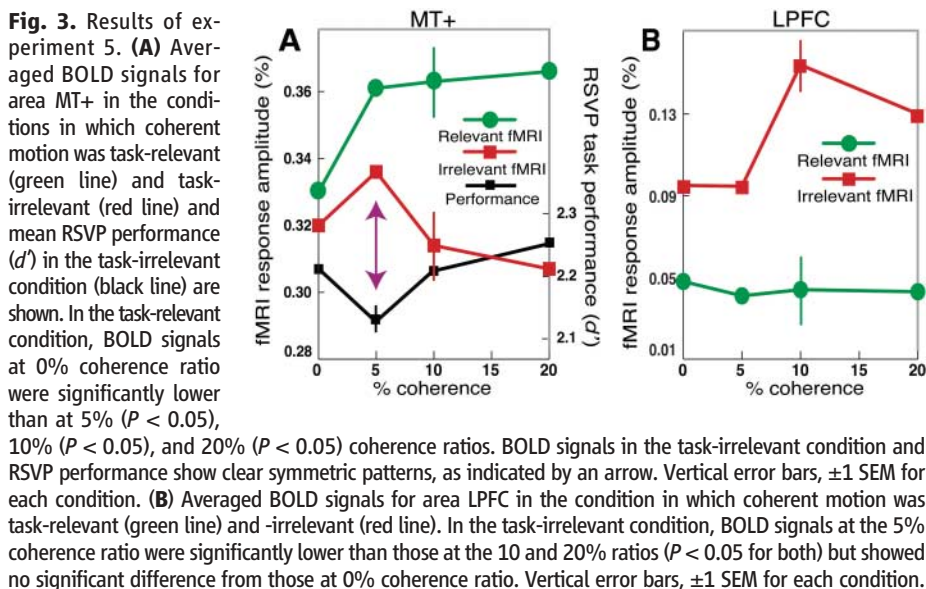
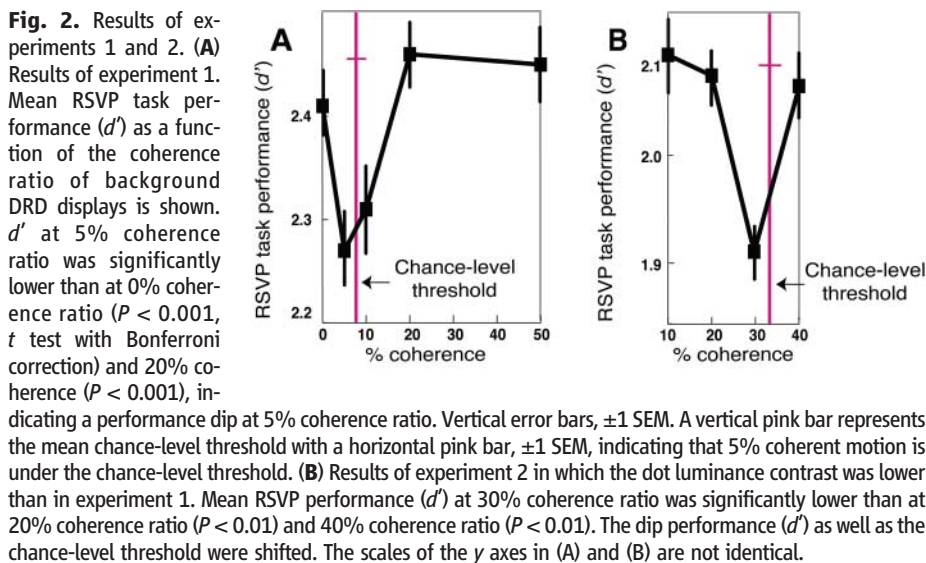
In experiment 2, to examine whether the performance dip and motion coherence threshold are correlated, we lowered the luminance contrast of the moving dots (from 65.9 to 2.2 candelas/m²) so that the coherence threshold would considerably increase, while maintaining the same methods used in the previous experiment ($n = 10$ participants). Both the threshold of coherent motion and the performance dip shifted toward a higher coherence ratio (Fig. 2B).

There is the possibility that task-irrelevant, translating coherent motion may induce eye movements, which could be related to the performance dip. In experiment 3 ($n = 6$), using the same method as in experiment 1 except that eye movements were monitored, the same pattern of performance was obtained. No systematic difference was observed in eye-movement patterns between coherence ratios (16). We also conducted experiment 4 ($n = 15$) in which signal dots contracted rather than translated, because contracting motion does not elicit major eye movements. Nevertheless, basically the same pattern of results was obtained, including the performance dip at the 5% coherence ratio (16). Thus, it does not seem that eye movements are a major factor in the performance-dip effect.

In experiment 5, to investigate the underlying neural mechanism that causes such a paradoxical effect, we measured fMRI activity in six partic-

ipants, with contracting coherent motion ratios varied between 0, 5, 10, and 20%. The amount of activity of MT+, which reflects the strength of processed motion signals (18), was highest for 5% coherence (Fig. 3A, red), at which level the performance dip occurred (Fig. 3A, black). Weak coherent motion that is around the chance-level threshold thus strongly activates MT+ and also impairs task performance. In contrast, the results of the control condition in which motion was task-relevant (16) show that the MT+ activity (Fig. 3A, green) and performance increased with increasing coherence ratio, which is in accord with previous findings (17, 18). Thus, the performance dip and highest MT+ activity are related to the fact that motion was task-irrelevant.

In the lateral prefrontal cortex (LPFC), which plays an important role in inhibitory control of inappropriate behavior or irrelevant signals (22–26), the amount of activity at the 5% coherence ratio showed no significant difference from that at 0% coherence but was significantly lower than at the 10 and 20% coherence levels (Fig. 3B, red) (27).



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How is the LPFC activity related to the activity in MT+ in the task-irrelevant condition? The correlation coefficient between the task-irrelevance-related activity (28) in MT+ and the LPFC was -0.90 . This is in accord with the view that when the LPFC is activated, it provides direct or indirect inhibitory control on the activity of MT+.

One might think that the low performance at the 5% coherence ratio was obtained because, despite the instructions to focus on RSVP task performance, the participants may have tried to find a coherent motion direction or to detect whether coherent motion was presented. If these motion tasks are difficult, they may leave fewer resources available for the RSVP task. However, this is not likely. If the participants engaged in the search for motion direction, this task should be hardest at 0% coherence and therefore, the lowest RSVP performance should have occurred at 0% and not at 5% coherence. Second, if the participants engaged in motion detection, this task should be hardest at 5% coherence because indecision may be greatest near the coherent motion threshold, and thus in accordance with the observed RSVP performance result. However, the lowest blood oxygen level-dependent (BOLD) activity was observed at 5% coherence ratio in the LPFC and cannot be directly explained by this possibility.

The results of the present study demonstrate two important points. First, a weak task-irrelevant stimulus feature that is below but near the perceptual threshold more strongly activates the visual area (MT+) that is highly related to the stimulus feature and more greatly disrupts task performance. There was a tendency for activity in the posterior occipitotemporal sulcus (pOTS) (29, 30) and the left angular gyrus (31), which are sensitive to letters and words and may be related to the RSVP task, to be lower at the 5% coherence than at the other coherent motion ratios. This contradicts the general view that irrelevant signals that are stronger in stimulus properties have a greater influence on the brain and performance and that the influence of a subthreshold stimulus is smaller than that of a suprathreshold stimulus.

Second, the results may reveal important bidirectional interactions between a cognitive controlling system and the visual system. The LPFC, which has been suggested to provide inhibitory control on task-irrelevant signals (22–26), may have a higher detection threshold for incoming signals than the visual cortex. Task-irrelevant signals around the threshold level may be sufficiently strong to be processed in the visual system but not strong enough for the LPFC to notice and, therefore, to provide effective inhibitory control on the signals (Fig. 4A). In this case, such signals may remain uninhibited, take more resources for a task-irrelevant distractor, leave fewer resources for a given task (32, 33), and disrupt task performance more than suprathreshold signals. On the other

hand, suprathreshold coherent motion may be noticed, may be given successful inhibitory control by the LPFC, and may leave more resources for a task (Fig. 4B) (22–26). This mechanism may underlie the present paradoxical finding that subthreshold task-irrelevant stimuli activate the visual area strongly and disrupt task performance more than some suprathreshold stimuli. It could also be one of the reasons why subthreshold stimuli often lead to relatively robust effects (2, 11, 14).

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Supporting Online Material

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Figs. S1 and S2
References

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Maternal Oxytocin Triggers a Transient Inhibitory Switch in GABA Signaling in the Fetal Brain During Delivery

Roman Tyzio,¹ Rosa Cossart,¹ Ilgam Khalilov,¹ Marat Minlebaev,¹ Christian A. Hübnér,² Alfonso Represa,¹ Yehezkel Ben-Ari,^{1*} Rustem Khazipov¹

We report a signaling mechanism in rats between mother and fetus aimed at preparing fetal neurons for delivery. In immature neurons, γ -aminobutyric acid (GABA) is the primary excitatory neurotransmitter. We found that, shortly before delivery, there is a transient reduction in the intracellular chloride concentration and an excitatory-to-inhibitory switch of GABA actions. These events were triggered by oxytocin, an essential maternal hormone for labor. In vivo administration of an oxytocin receptor antagonist before delivery prevented the switch of GABA actions in fetal neurons and aggravated the severity of anoxic episodes. Thus, maternal oxytocin inhibits fetal neurons and increases their resistance to insults during delivery.

Delivery is a stressful event associated with high risks to the fetal brain (1); however, whether the fetal brain prepares for

delivery remains largely unknown. We addressed this issue by studying γ -aminobutyric acid (GABA)-mediated (GABAergic) signaling in the