## RSNA Press Release

# Methylene Blue Shows Promise for Improving Short-Term Memory

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At A Glance

- Researchers used fMRI to identify changes in the brains of study participants after one low dose of methylene blue.
- The results showed an increased response in regions of the brain related to short-term memory and attention and a 7 percent increase in memory retrieval.
- The results may provide a foundation for future trials of methylene blue in cognitive impairment, dementia and other conditions that might benefit from drug-induced memory enhancement.

OAK BROOK, Ill. — FA single oral dose of methylene blue results in an increased MRI-based response in brain areas that control short-term memory and attention, according to a new study published online in the journal *Radiology*.

Methylene blue is used to treat methemoglobinemia, a blood disorder in which oxygen is unable to release effectively to body tissues, and as a surgical stain.

Animal studies have shown a single low dose of methylene blue enhances long-term contextual memory—the conscious recall of the source and circumstances of a specific memory—and extinction memory, a process in which a conditioned response from stimuli gradually diminishes over time.

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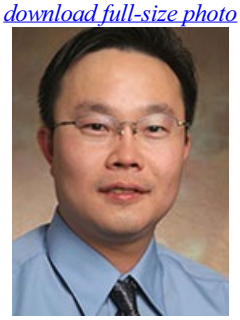

*Timothy Q. Duong, Ph.D.*

"Although the memory-enhancing effects of methylene blue were shown in rodents in the 1970s, the underlying neuronal changes in the brain responsible for memory improvement and the effects of methylene blue on short-term memory and sustained-attention tasks have not been investigated," said study author Timothy Q. Duong, Ph.D., from the University of Texas Health Science Center at San Antonio, Texas. "Our team decided to conduct the first multi-modal MRI study of methylene blue in humans."

Twenty-six healthy participants, between the ages of 22 and 62, were enrolled in a double-blinded, randomized, placebo-controlled clinical trial to measure the effects of methylene blue on the human brain during working-memory and sustained-attention tasks. This study was approved by the local ethical committee.

The participants underwent functional MRI (fMRI) before and one hour after low-dose methylene blue or placebo administration to evaluate the potential effects of methylene blue on cerebrovascular reactivity during tasks. Mean cerebral blood flow was measured pre- and post-intervention.

The results showed methylene blue increased response in the bilateral insular cortex—an area deep within the brain associated with emotional responses—during a task that measured reaction time to a visual stimulus. The fMRI results also showed an increased response during short-term memory tasks involving the brain's prefrontal cortex, which controls processing of memories, the parietal lobe, primarily associated with the processing of sensory information, and the occipital cortex, the visual processing center of the brain. In addition, methylene blue was associated with a 7 percent increase in correct responses during memory retrieval.

The findings suggest that methylene blue can regulate certain brain networks related to sustained attention and short-term memory after a single oral low dose.

"This work certainly provides a foundation for future trials of methylene blue in healthy aging, cognitive impairment, dementia and other conditions that might benefit from drug-induced memory enhancement," Dr. Duong said.

"Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain." Collaborating with Dr. Duong were Pavel Rodriguez, M.D., Wei Zhou, B.S., Douglas W. Barrett, Ph.D., Wilson

Altmeyer, M.D., Juan E. Gutierrez, M.D., Jinqi Li, M.D., Jack L. Lancaster, Ph.D., and Francisco Gonzalez-Lima, Ph.D.

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For patient-friendly information on brain MRI, visit *RadiologyInfo.org*.

Images (JPG, TIF):

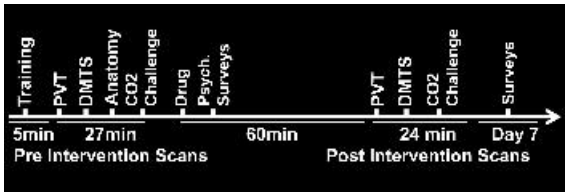


**Figure 1.** Schematic shows the timeline of functional MR imaging and surveys, including psychomotor vigilance task *(PVT)* and delayed match-to-sample *(DMTS)* task.

High-res (TIF) version

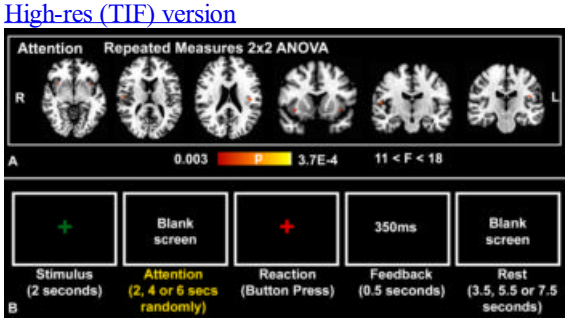


**Figure 2.** Psychomotor vigilance Task. A, Repeated-measures analysis of variance (ANOVA) results of the attention phase of the psychomotor vigilance task superim¬posed to a standard brain template (colors indicate P values of significant voxels, cluster-based $P < .05$; cluster size, $K \geq 10$) shows positive drug X time interactions in favor of a methylene blue effect in the bilateral anterior and posterior insular cortices ($n = 26$, with 24 degrees of freedom). B, Representative block from the psychomo¬tor vigilance task shows the stimulus, attention, reaction, feedback, and rest phases as demarcated by set times.

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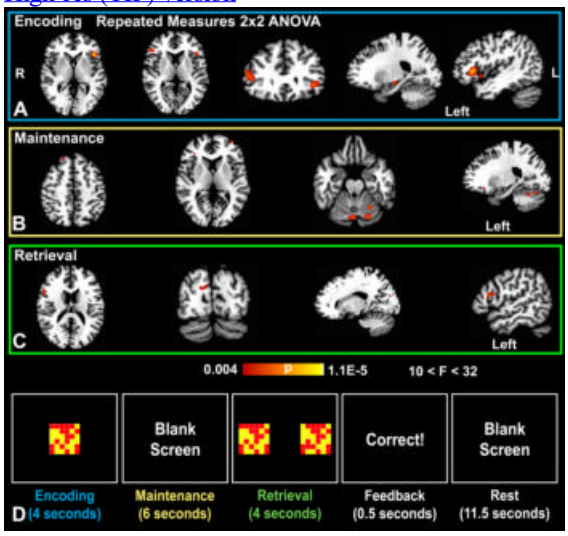


**Figure 3.** Delayed match-to-sample task. Repeated-measures ANOVA results of the delayed match-to-sample task (colors indicate P values of significant voxels, cluster-based $P < .05$; $K \geq 10$) superimposed to a standard brain

template. A, Probability map overlays show positive drug X time interactions in favor of a methy¬lene blue effect in the bilateral inferior frontal gyri during the encoding phase, B, in the right superior frontal gyrus, left middle frontal gyrus, and posterior cerebellum during the maintenance phase, and, C, in the right inferior frontal gyrus and cuneus during the retrieval phase (n = 26, with 24 degrees of freedom). D, Representa¬tive blocks from the delayed match-to-sample task show the encoding, maintenance, retrieval, feedback, and rest phases as demarcated by set times.

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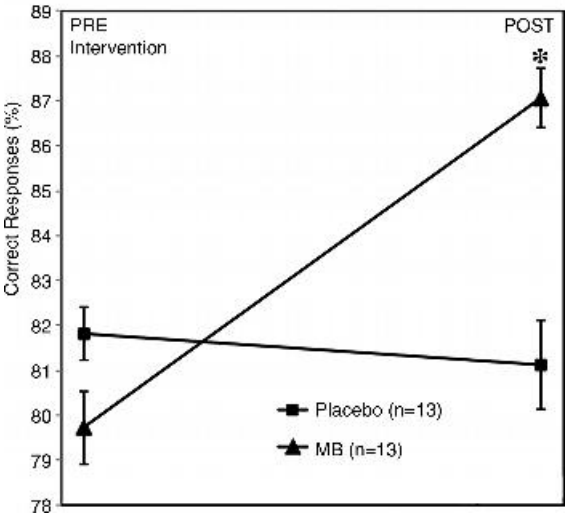


**Figure 4.** Analysis of delayed match-to-sample task performance change (after intervention to before intervention) during the retrieval phase shows a significant increase in correct responses only in the methylene blue *(MB)* group ($P = .01$). Error bars = standard error of mean.

High-res (TIF) version

Resources:

Study abstract