Memory, depression, insomnia -- and worms?

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Researchers have spent decades probing the causes of depression, schizophrenia and insomnia in humans. But a new study may have uncovered key insights into the origins of these and other conditions by examining a most unlikely research subject: worms.

The project, which was led by Oklahoma Medical Research Foundation scientist Kenneth Miller, Ph.D., examined the way eye-less microscopic worms known as C. elegans shy away from certain kinds of light. The researchers made several key findings, chief among them that exposing paralyzed C. elegans to ultraviolet light restored normal levels of movement in the worms.

Miller's group at OMRF traced the light reaction to a tiny molecular sensor, which is encoded by a gene they named LITE-1. "This sensor doesn't resemble any other light sensors previously discovered," said Miller.

Although humans lack this ultraviolet light sensor, Miller's discovery provides a window for understanding how the molecular signals in our nerve cells allow them to talk to each other to produce perceptions, behaviors, learning and memory.

"That doesn't mean shining an ultraviolet light on people in wheelchairs will suddenly allow them to walk," said Miller. "But it does give us a tool that we can use to solve the mysteries of nerve cell communication and could ultimately help us understand the biology of everything from sleep and memory to depression."

The research appears in the Aug. 5, 2008 edition of the journal *PLoS Biology*.

"The new work from Ken Miller's lab has identified a new way that organisms can sense light, distinct from the previously known light-sensing mechanism used in the eye," said Michael Koelle, Ph.D., of the Yale University School of Medicine. "It will be interesting to see whether the LITE-1 light-sensing mechanism will also lead to new insights into human sensory perception."

Despite 35 years of intensive research by hundreds of labs studying C. elegans, no one had discovered that eye-less worms can respond robustly to light. Miller's group found the light response when they began studying worms that were paralyzed because of a gene mutation.

In prior studies, Miller and his OMRF colleagues showed that this mutation disrupts a molecular network of pathways that controls how nerve cells send signals to each other at synapses, the points where different neurons touch each other. Those same nerve cell pathways are all present in the human brain, where they are thought to play a role in controlling behaviors, learning and memory, and may also be involved in causing human neurological disorders.

"Without signals from this network, neurons cannot talk to each other or to muscle cells to produce movement, so the mutants just lie paralyzed on the culture plate even if you poke and prod them," Miller said.

But when Miller turned a short wavelength light—like ultraviolet rays—on the worms, it created a new signal in the neurons, allowing the animals to move as long as the light was on them. The same response had not been found previously in normal C. elegans because those worms have no trouble moving.

Miller said he thinks the worms are hardwired to avoid damaging or lethal doses of direct sunlight, which includes UV rays.

"When you are only a few cells thick, getting a sunburn is fatal," he said.

Miller emphasized that the research is still in its early stages. "We're a long way from any treatments based on this research, but I think we've opened up a door that we didn't know was there before," he said. "There's a lot of work left to be done, but I'm excited to see where this discovery leads us."

Source: Oklahoma Medical Research Foundation