

Researchers uncover biochemical events needed to maintain erection

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For two decades, scientists have known the biochemical factors that trigger penile erection, but not what's needed to maintain one. Now an article by Johns Hopkins researchers, scheduled to be published this week by the *Proceedings of the National Academy of Sciences (PNAS)*, uncovers the biochemical chain of events involved in that process. The information, they say, may lead to new therapies to help men who have erectile dysfunction.

"We've closed a gap in our knowledge," says Arthur Burnett, M.D., professor of urology at Johns Hopkins Medicine and the senior author of the study article. "We knew that the release of the chemical [nitric oxide](#), a neurotransmitter that is produced in [nerve tissue](#), triggers an erection by relaxing muscles that allow blood to fill the penis. We thought that was just the initial stimulus. In our research, we wanted to understand what happens next to enable that erection to be maintained."

In a study of mice, Burnett and his colleagues found a complex positive feedback loop in the penile nerves that triggers waves of nitric oxide to keep the penis erect. He says they now understand that the [nerve impulses](#) that originate from the brain and from [physical stimulation](#) are sustained by a cascade of chemicals that are generated during the erection following the initial release of nitric oxide. "The basic biology of erections at the rodent level is the same as in humans," he says.

The key finding is that after the initial release of nitric oxide, a biochemical process called phosphorylation takes place to continue its

release and sustain the erection.

In a landmark study published in the [journal Science](#) in 1992, Burnett and his Johns Hopkins co-author, Solomon S. Snyder, M.D., professor of neuroscience (who is also an author on the current study), showed for the first time that nitric oxide is produced in penile tissue. Their study demonstrated the key role of nitric oxide as a neurotransmitter responsible for triggering erections.

"Now, 20 years later, we know that nitric oxide is not just a blip here or there, but instead it initiates a cyclic system that continues to produce waves of the [neurotransmitter](#) from the penile nerves," says Burnett.

With this basic biological information, it may be possible, according to Burnett, to develop new medical approaches to help men with erection problems caused by such factors as diabetes, vascular disease or nerve damage from surgical procedures. Such new approaches could be used to intervene earlier in the arousal process than current medicines approved to treat erectile dysfunction.

In particular, Burnett says, "The target for new therapies would be the protein kinase A (PKA) phosphorylation of neuronal nitric oxide synthase (nNOS). Now that we know the mechanism for causing the 'activated' form of nNOS in penile nerves, we can develop agents that exploit this mechanism to help with erection difficulties."

One of the agents studied by the researchers was forskolin, an herbal compound that has been used to relax muscle and widen heart vessels. They found that forskolin also ramps up nerves and can help keep nitric oxide flowing to maintain an [erection](#).

"It has been a 20-year journey to complete our understanding of this process," says Snyder. "Now it may be possible to develop therapies to

enhance or facilitate the process."

More information: "Cyclic AMP Dependent Phosphorylation of Neuronal Nitric Oxide Synthase Mediates Penile Erection," *Proceedings of the National Academy of Sciences*, 2012.

Provided by Johns Hopkins University School of Medicine

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