New test quickly identifies patients whose postoperative pain can be effectively treated by hypnosis

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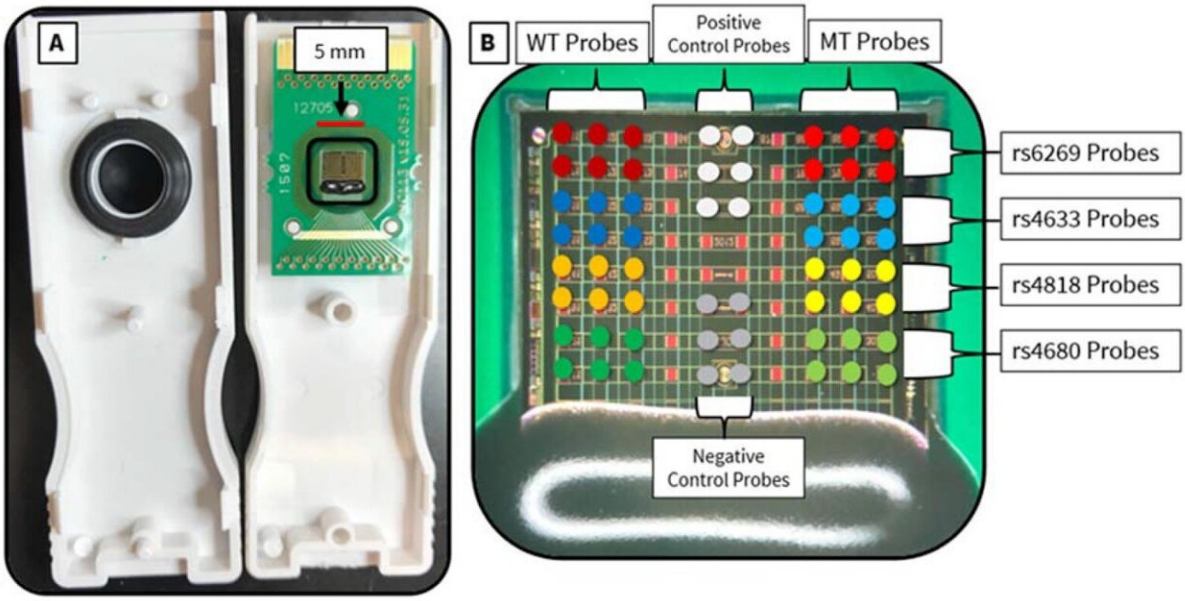

A: Giant magnetoresistive (GMR) biosensor array in its reusable cartridge. The black boxed area indicates the region magnified and displayed in B. The red line is inserted for scale. The GMR biosensor is 5 mm in length. B: A zoomed-in image of the GMR biosensor array overlaid with the pattern of functionalized probes on the surface of the individual sensors. The chip hosts an array of 80 individually addressable GMR biosensors, which can be seen in the image as red squares, some of which are covered by the overlaid pattern of probes. Each sensor can be individually functionalized with capture probes and is addressed and measured during readouts for sensor-specific changes in resistance due to the GMR effect. Credit: Dana L. Cortade and Shan X. Wang

Hypnosis is an effective treatment for pain for many individuals but determining which patients will benefit most can be challenging. Hypnotizability testing requires special training and in-person evaluation is rarely available in the clinical setting. Now, investigators have developed a fast, point-of-care molecular diagnostic test that identifies a subset of individuals who are most likely to benefit from hypnosis interventions for pain treatment.

Their study, in *The Journal of Molecular Diagnostics*, also found that a subset of highly hypnotizable individuals may be more likely to experience high levels of postoperative pain.

"Since hypnotizability is a stable cognitive trait with a genetic basis, our goal was to create a molecular diagnostic tool for objectively identifying individuals who would benefit from hypnosis by determining 'treatability' at the point-of-care," explained co-lead investigator Dana L. Cortade, a recently graduated Ph.D. in Materials Science and Engineering, School of Engineering, Stanford University, Stanford, CA, U.S.. "The advancement of nonpharmacological adjuvant treatments for pain is of the utmost importance in light of the opioid epidemic."

Prior research established that the genetic basis for hypnotizability includes four specific single-nucleotide polymorphisms (SNPs), or genetic variations, found in the catechol-o-methyltransferase (COMT) gene for an enzyme in the brain that is responsible for dopamine metabolism in the prefrontal cortex. Although SNPs can contain valuable information on disease risk and treatment response, widespread use in clinical practice is limited because of the complexities, costs, and time delays involved in sending samples to laboratories for testing.

The investigators developed a SNP genotyping assay on a giant

magnetoresistive (GMR) biosensor array to detect the optimal combination of the COMT SNPs in patient DNA samples. GMR biosensor arrays are reliable, cheaper, sensitive, and can be easily deployed in point-of-care settings using saliva or blood samples.

The study investigated the association between COMT diplotypes and hypnotizability using a clinical hypnotizability scale called the Hypnotic Induction Profile (HIP) in individuals who had participated in one of the three previous clinical trials in which an HIP was administered. An additional exploratory study of the association between perioperative pain, COMT genotypes, and HIP scores was conducted with the patients in the third cohort, who had undergone total knee arthroplasty (TKA).

DNA was extracted from blood samples previously collected in the first cohort, and saliva samples were collected by mail from participants in the other two trials. Participants were considered treatable by hypnosis if they had HIP scores of 3 or higher on a scale of zero to 10.

For participants identified with the optimal COMT diplotypes by the GMR biosensor array, 89.5% scored highly on the HIP, which identified 40.5% of the treatable population. The optimal COMT group mean HIP score was significantly higher than that in the suboptimal COMT group. Interestingly, further analysis revealed that the difference was observed only in women.

"Although we had expected some difference in effect between females and males, the association between hypnotizability and COMT genotypes was strongest in the females in the cohort," said co-lead investigator Jessie Markovits, MD, Department of Internal Medicine, Stanford School of Medicine, Stanford, CA, U.S..

"The difference may be due to lower numbers of males in the cohort, or because COMT is known to have interactions with estrogen and to differ

in activity by sex. Additional gene targets including COMT, with stratification by sex, could be the focus of future study."

In the exploratory analysis of the relationship between COMT genotypes and pain after TKA surgery, the same optimal COMT individuals had significantly higher postoperative pain scores than the suboptimal group, indicating a greater need for treatment.

"This supports the body of evidence that COMT genotypes impact pain, and it is also known that COMT genotypes affect opioid use after surgery. Pain researchers can use this technology to correlate genetic predisposition to pain sensitivity and opioid use with response to an evidence-based, alternative remedy: hypnosis," Dr. Cortade said.

COMT SNPs alone are not a complete biomarker for identifying all individuals who will score highly on a hypnotizability scale and experience high pain sensitivity. The GMR sensor nanoarray can accommodate up to 80 SNPs, and it is possible that other SNPs, such as those for dopamine receptors, are needed to further stratify individuals.

The investigators observe that this study highlights the utility and potential of the evolving applications of precision medicine. "It is a step towards enabling researchers and healthcare professionals to identify a subset of patients who are most likely to benefit from hypnotic analgesia," Dr. Markovits said.

"Precision medicine has made great strides in identifying differences in drug metabolism that can impact medication decisions for perioperative pain. We hope to provide similar precision in offering hypnosis as an effective, non-pharmacological treatment that can improve patient comfort while reducing opioid use."

More information: Dana L. Cortade et al, Point-of-Care Testing of

Enzyme Polymorphisms for Predicting Hypnotizability and Postoperative Pain, *The Journal of Molecular Diagnostics* (2023). DOI: 10.1016/j.jmoldx.2023.01.002