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Imaging in Medicine

News & Views

News

Research Highlights

Imaging technique used to visualize brain activity associated with chronic low back pain

New research has demonstrated correlate neural activity with back pain in patients using the technique arterial spin labeling. The work was performed by a group of pain management researchers at Harvard Medical School (Boston, MA, USA) and published recently in *Anesthesiology*.

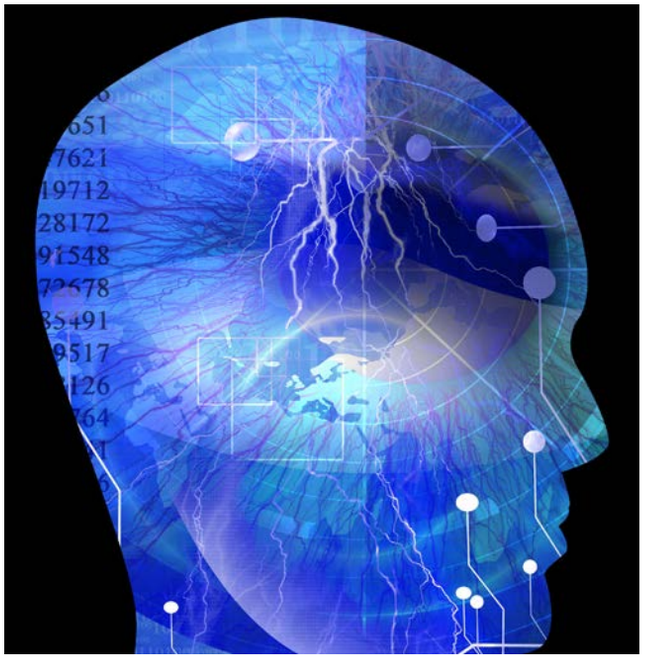
"...pain is a very personal experience, which is impossible for a patient to communicate accurately to a clinician. The aid of imaging technology in pain assessment would no doubt have an immense positive impact in this field."

Owing to its varying nature, chronic pain (CP) is difficult to correlate to neural activity using conventional functional MRI. In addition, pain is a very personal experience, which is impossible for a patient to communicate accurately to a clinician. The aid of imaging technology in pain assessment would no doubt have an immense positive impact in this field.

Arterial spin labeling is a perfusion-based method of functional MRI. This technique allows the absolute quantification of regional cerebral blood flow, which is the measure of neuronal activity. The resulting image is a 'cerebral perfusion map', which can be achieved without the administration of a contrast agent or ionizing radiation. This is because this technique uses magnetically labeled endogenous blood water as a freely diffusible tracer.

So how do the changes detected by arterial spin labeling correlate with low back pain? Lead author of the study, Ajay Wasan, explains, "We've found that when a patient has worsening of their usual pain, there are changes in the activity of the brain. These changes occur in the network of areas in the brain that process pain and mood."

This study looked at participants with chronic low back and radicular pain and also healthy normal subjects. The subjects partook in three sessions: a characterization and training session and two arterial spin labeling sessions. In the first imaging session, CP was exacerbated using clinical maneuvers such as pelvic tilting or straight leg rising. In the second and third sessions,



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noxious heat was applied to the affected area of pain. Arterial spin labeling was used throughout to measure brain activity associated with their CP.

The results demonstrated that arterial spin labeling displayed significant changes in neuronal activity during the first session in subjects with low back pain. The healthy controls displayed no significant changes in any of the sessions. These differences in neurological activity were not observed after administration of noxious heat to any of the patients, nor in any task involving the healthy subjects. These results indicate that arterial spin labeling displayed neural processing that was specific to only CP.

The clinically significant worsening of ongoing CP (less than or equal to 30%, n = 16) was associated with significant regional blood flow increases (6–10 mm/100 g of tissue/min, $p < 0.01$) within brain regions known to activate with experimental pain (somatosensory, prefrontal and insular cortices) and in other structures observed less frequently in experimental pain studies, such as the superior parietal lobule (part of the dorsal attention network). This effect is specific to changes in ongoing CP as it is observed during worsening CP, but it is not observed after thermal pain application, or in matched, pain-free healthy controls.

The study authors believe that this research warrants further investigation into the link between neuronal activity and peripheral pain. Wasan speaks about future research directions: "While this study begins to uncover some of the basic physiology of the brain as it processes pain, more studies are needed to help us understand how the brain function may change over the course of treatment of pain and to examine the brain mechanisms by which pain improves."

Wasan comments on the potential value of this research: "We are getting closer to describing, on an objective level, how the body and brain are reacting when a patient reports having more pain. We are hopeful that this could lead to an understanding of an individual patient's neurocircuitry and that knowledge could lead to therapies that would be tailored to the individual."

Wasan and colleagues hope that these findings are a step towards finding standard biomarkers for the CP experience.

Source: Wasan AD, Loggia ML, Chen LQ, Napadow V, Kong J, Gollub RL. Neural correlates of chronic low back pain measured by arterial spin labeling. Anesthesiology *115(2), 364–374 (2011).*

PET used to image amyloid levels in patients with Alzheimer's disease

A recent study, published in the *Archives of Neurology*, has further demonstrated the utility of fluorine-18-labeled radiotracers used with PET in detecting and quantifying β-amyloid (Aβ) in the brain, a pathological hallmark of Alzheimer's disease (AD).

In the former, the researchers working across multiple research imaging centers, aimed to characterize florbetapir F 18 measurements of fibrillar Aβ in a large clinical cohort of 68 participants with probable AD, 60 with mild cognitive impairment (MCI) and 82 older healthy controls. Cerebral-to-whole-cerebellar florbetapir standard uptake value ratios (SUVRs) were calculated to allow comparison of mean cortical SUVRs. Pathological amyloid thresholds and SUVRs were calibrated based on separate antemortem PET and postmortem neuropathology data from 19 end-of-life patients.

All of the participant groups had significantly different mean cortical florbetapir SUVRs; the highest were in individuals with probable AD (1.39) and the lowest in healthy controls (1.05). The same pattern was found in comparison to percentage meeting levels of amyloid associated with AD by SUVR criteria, and in percentage meeting SUVR criteria for the presence of any identifiable Aβ. Florbetapir uptake increased with age in healthy individuals and was higher in those who carried the APOE-4 allele.

> "...florbetapir PET can distinguish clinical stages of AD, and can identify amyloid pathology in a percentage of cognitively normal individuals over the age of 55."

The study by Fleisher *et al.* builds from a previous study and confirms the ability of florbetapir-PET SUVRs to characterize amyloid levels in clinically probable AD, MCI, and older healthy control groups using continuous and binary measures of fibrillar Aβ burden. This latest study confirms the ability of flobetapir PET "to distinguish clinical syndromes of AD, as well as identify the degree of abnormality seen in normal aging populations – potential preclinical AD", explains lead author Adam Fleisher, Associate Director of brain imaging at the Banner Alzheimer's Institute (Phoenix, AZ, USA). Moreover, the study "also introduces thresholds of florbetapir PET levels associated with having 'any amyloid' in the brain, or levels associated with pathologically proven dementia of the Alzheimer's type", he adds.

Fleisher concludes that "florbetapir PET can distinguish clinical stages of AD, and can identify amyloid pathology in a percentage of cognitively normal individuals over the age of 55". The study "presents compiled data for several registered trials documenting its ability to distinguish between diagnostic groups, and establishes clinically relevant thresholds of PET activity."

Source: Fleisher AS, Chen K, Liu X et al. *Using positron emission tomography and florbetapir F 18 to image cortical amyloid in patients with mild cognitive impairment or dementia due to Alzheimer disease.* Arch. Neurol. *doi: 10.1001/archneurol.2011.150 (2011) (Epub ahead of print).*

Novel breast cancer mammography technique shows promising *ex vivo* results

A group of researchers at the Scherrer Institute (Villigen, Switzerland) are developing a new breast cancer diagnostic technique that is hoped to allow clinicians to see structures that are not picked up by conventional mammography. These findings were recently published in *Investigative Radiology*.

A problem with conventional mammography procedures is that they only determine the extent to which x-rays are attenuated by various tissue structures. This means that often structures in the breast may be missed. The method adopted in this study, phase-contrast and scattering-based x-ray imaging, is known to provide additional and complementary information to conventional imaging methods. This is because it makes use of the fact that x-rays actually consist of waves, and that their properties change slightly as they travel through tissue. The device measures these changes, and consequently can contribute a more meaningful image of the breast tissue.

Research has shown that in this new procedure x-rays pass through the breast in exactly the same way as in traditional mammography. The difference is that a conventional x-ray image can only determine how much of the beam has been retained by the tissue. The technique used in this study recognizes that x-rays also undergo another subtle change; x-rays are electromagnetic waves, and as they pass through various tissue structures the direction of the waves undergoes slight changes.

Ewald Rössl, project manager for this work at Philips Healthcare (Best, The Netherlands), explained: "The potential of this method is defined on the one hand by the innovative nature of the measured information, but on the other hand is also characterized by the use of conventional technologies that are widely applied in medical technology to generate and detect x-rays. Our declared goal is to use the example of mammography on human beings to conclusively demonstrate the clinical benefits."

Scientists from the research department at Philips Healthcare are also currently investigating the use of this imaging method for application in other medical practices, although the focus is particularly on mammography. A clinical study is currently underway, in which the researchers hope to confirm if this new diagnostic method provides any benefit to a large group of patients.

Source: Stampononi M, Wang Z, Thüring T et al. *The first analysis and clinical evaluation of native breast tissue using differential phase-contrast mammography.* Invest. Radiol. *doi: 10.1097/RLI.0b013e31822a585f (2011) (Epub ahead of print).*

Novel screening method for pancreatic cancer shows hope for earlier detection

A study published recently in *Gastrointestinal Endoscopy* has reported that imaging the tumor marker serum CA 19–9 using endoscopic ultrasound could allow for detection of pancreatic cancer at an earlier stage. These finding were obtained from a prospective cohort study performed at the University of Vermont (Burlington, VT, USA) and the Dartmouth-Hitchcock Medical Center (Lebanon, NH, USA).

Pancreatic cancer is currently the fourth leading cause of cancer death in the USA, and research has shown that advanced disease at the time of diagnosis is linked to higher mortality. The group that performed this study proposed the objective to find a method of detecting pancreatic neoplasia at an early stage. If achieved, the hope would be to intervene earlier on in cancer progression and improve patients' chances of survival.

> "Stage 1 pancreatic cancer is more likely to be detected by using this screening protocol than by using standard means of detection."

Participants in this study were aged between 50 and 80 years and all had at least one first-degree relative with pancreatic adenocarcinoma, which significantly increases an individual's chances of developing the cancer by approximately two- to five-fold.

The study involved initially serum testing for levels of CA 19–9 in all patients. The subjects with elevated CA 19–9 were then screened using endoscopic ultrasound. Of the 456 individuals recruited for this study, 27 showed elevated CA 19–9. Ultrasound results found that out of these 27 subjects, five presented neoplastic or malignant lesions, and one presented pancreatic adenocarcinoma

Lead author, Richard Zubarik (University of Vermont), summarizes the significance of these findings: "Our results showed that potentially curative pancreatic adenocarcinoma can be identified with this screening protocol. Stage 1 pancreatic cancer is more likely to be detected by using this screening protocol than by using standard means of detection."

Source: Zubarik R, Gordon SR, Lidofsky SD et al. *Screening for pancreatic cancer in a high-risk population with serum CA 19–9 and targeted EUS: a feasibility study.* Gastrointest. Endosc. *74(1), 87–95 (2011).*

MRI-guided laser surgery used to treat epilepsy in children

Surgeons at the Texas Children's Hospital (Houston, TX, USA) have announced the first ever use of real-time MRI-guided thermal imaging and laser technology to destroy lesions that can lead to epileptogenic seizures.

Currently, the gold standard surgical treatment for epilepsy is craniotomy, a surgical operation in which a large portion of the skull is temporarily removed during the procedure. This newly performed technique in minimally invasive in comparison to craniotomy, as the MRI-guided laser probe is inserted through a tiny 3.2 mm hole in the skull. As a consequence patient recovery time is expected to be much shorter.

A further advantage of this method is that the probe utilizes a much smaller pathway through the brain to reach a deep lesion. This reduces the risk of complications resulting from contact with surrounding brain tissue.

> "The benefits of this new approach ... may open the door for more epilepsy patients to see surgery as a viable option."

Angus Wilfong (Texas Children's Hospital and Baylor College of Medicine) provides a hopeful view on the future of this procedure: "Based on our experience, we believe the use of MRI-guided laser surgery will change the face of epilepsy treatment and provide a life-changing option for many epilepsy surgery candidates, both children and adults … The benefits of this new approach … may open the door for more epilepsy patients to see surgery as a viable option."

Source: Texas Children's Hospital. News releases: Texas Children's Hospital pioneers use of MRI-guided laser surgery for revolutionary new epilepsy treatment. www.texaschildrens.org/allabout/news/2011/epilepsy_treatment.aspx (Accessed 19 August 2011).

About the News

The News highlights some of the most important events and research in the field of nanomedicine. If you have newsworthy information, please contact: Sam Rose, Commissioning Editor, *Imaging in Medicine,* s.rose@futuremedicine.com