Chronic Knee Pain Linked to Accelerated Brain Aging

A new study reveals that individuals with chronic musculoskeletal pain, particularly knee osteoarthritis, may experience faster brain aging compared to healthy people. The research, published in *Nature Mental Health* on March 26, used brain MRI data from over 9,000 individuals to develop an AI model that estimates brain age relative to chronological age (doi: 10.1038/s44220-024-00223-3).

Researchers led by Prof. TU Yiheng from the Institute of Psychology of the Chinese Academy of Sciences (IPCAS), in collaboration with international experts, found that knee osteoarthritis patients had brains that appeared older than their years, with regions crucial for cognition like the hippocampus displaying accelerated aging patterns, which could predict future memory decline and increased dementia risk.

The study points to the gene SLC39A8 as a link between knee osteoarthritis and brain aging and highlights inflammation and neurodevelopmental processes as potential underlying mechanisms. Beyond shedding light on the cognitive impacts of chronic pain, this multidisciplinary collaboration opens avenues for early detection and intervention strategies targeting dementia risk factors stemming from musculoskeletal conditions.

Chronic pain leads to accelerated brain aging. (Image by XIE Rui)

The study provides a wake-up call on the far-reaching effects of chronic pain, underscoring the urgency of developing effective pain management approaches to safeguard brain health during aging.

Empathy is Contagious

How much we care about someone else's pain depends a lot on the people around us. In a series of experiments, Dr. ZHOU Yuqing from the Institute of Psychology of the Chinese Academy of Sciences (IPCAS) and her team found that people's empathy – their ability to share and understand others' feelings of pain – could be changed by watching how empathetic or uncaring others were (doi: 10.1073/pnas.2313073121). The results were published in *PNAS* on February 21.

New study reveals that empathy can be socially transmitted. (Image by American Psychological Association)

If people observed someone reacting with high empathy and concern towards another person's suffering, it caused the observers themselves to become more empathetic. Their ratings of how badly they felt for the suffering person increased after seeing an empathetic reaction. However, if they saw someone react without much empathy or concern for the person in pain, the observers lowered the ratings of their own empathy.

Importantly, these changes in empathetic feelings

were reflected in the observers' brain activity. Seeing highly empathetic reactions activated the communication between brain regions involved in learning from observations and regions that process empathy for pain. In contrast, observing low empathy suppressed this brain communication.

The researchers could even predict how much an individual's empathy would change based on a computational learning model that tracked the discrepancy between the observer's expectations and the empathetic responses they witnessed.

In summary, the findings reveal a neural mechanism for how empathy can spread through social interactions when we see caring behavior, but diminish when we are surrounded by indifference to others' suffering. Empathetic environments seem to cultivate compassion, while callous company can numb our sensitivity to others' pain.

Estimating Biological Age with DNA Methylation Clocks

Recently, a research team led by researchers from the Beijing Institute of Genomics and Institute of Zoology, both under the Chinese Academy of Sciences, and their collaborators from the Quzhou Affiliated Hospital of Wenzhou Medical University developed innovative epigenetic clocks specifically for Chinese populations, offering a more tailored approach to measuring biological age among Chinese population (doi: 10.1093/procel/pwae011).

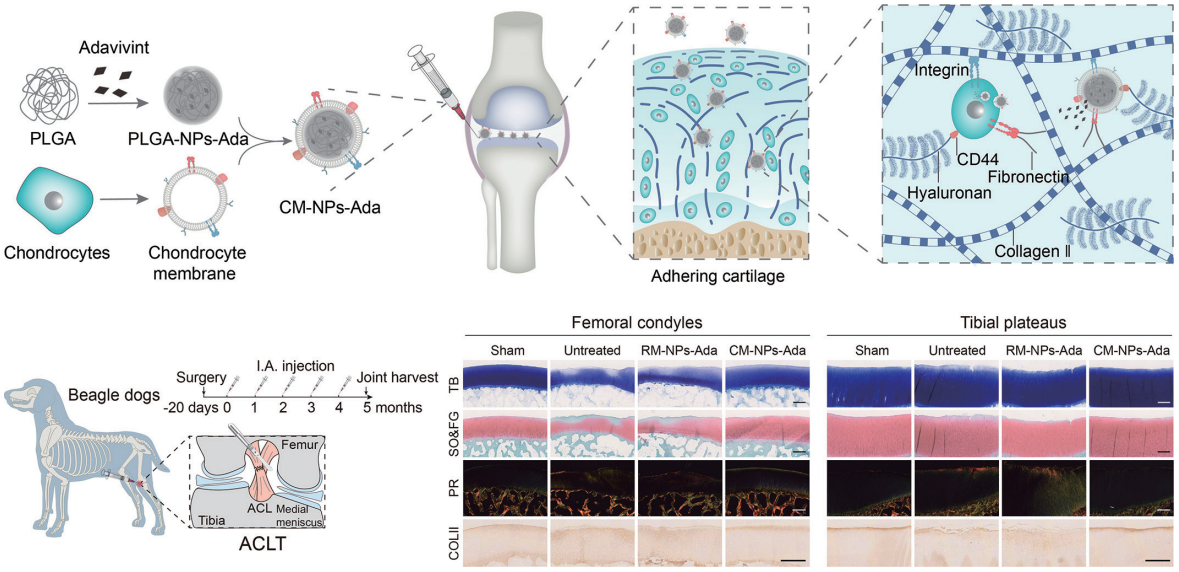
These tools, detailed in the journal *Protein Cell*, use DNA methylation a biochemical process that adds a methyl group to DNA, affecting gene expression without changing the DNA sequence itself at specific sites in the genome to more accurately predict age and assess connections between aging, lifestyle, and disease.

Unlike the previously reported biological clock, this innovative method takes ethnic differences into account. It provides a more precise assessment of the impact of lifestyle and disease on the aging process among the Chinese population and enhances the potential for personalized medical interventions focused on aging and associated health issues.

Scientists developed a DNA Methylation Clock to estimate the biological age of the Chinese population. (Image created using DALL-E by YAN F.)

Nano "Undercover Agents" Lodge in Cartilage to Treat Osteoarthritis

The relentless pain and disability caused by osteoarthritis stem from the body's own cartilage cells going rogue under inflammatory conditions. They secrete enzymes that devour the cushioning cartilage matrix,



The preparation process of chondrocyte-mimicking nanotherapeutics, mechanism of action, and assessment of efficacy in large animal models (Image by NIE Guangjun *et al.*)

leading to joint damage. Conventional drugs cannot effectively reach this inflammatory source within the dense cartilage.

Now, a research team led by Prof. NIE Guangjun from the National Center for Nanoscience and Technology (NCNST) of the Chinese Academy of Sciences and Prof. YU Jiakuo from the Tsinghua Changgung Hospital Medical Center of Tsinghua University have developed biomimetic nanoparticles that infiltrate the cartilage by mimicking the exterior of chondrocytes (doi:10.1126/scitranslmed.adh9751). These nano-decoys, loaded with anti-inflammatory drugs, latched onto cartilage fibrils thanks to their cell-like surface proteins. They established a persistent drug depot inside joints lasting for over a month while evading systemic clearance.

Remarkably, the nanocarriers not only delivered therapeutics but also disarmed the inflammatory chondrocytes through a payload that inhibits a particular signaling pathway. In osteoarthritic animal models, this treatment restored gait, reduced bone remodeling, and robustly protected cartilage from degeneration.

This innovative approach paves the way for long-acting osteoarthritis therapies and opens avenues for targeted drug delivery to other diseased tissues using biomimetic nanotechnology.