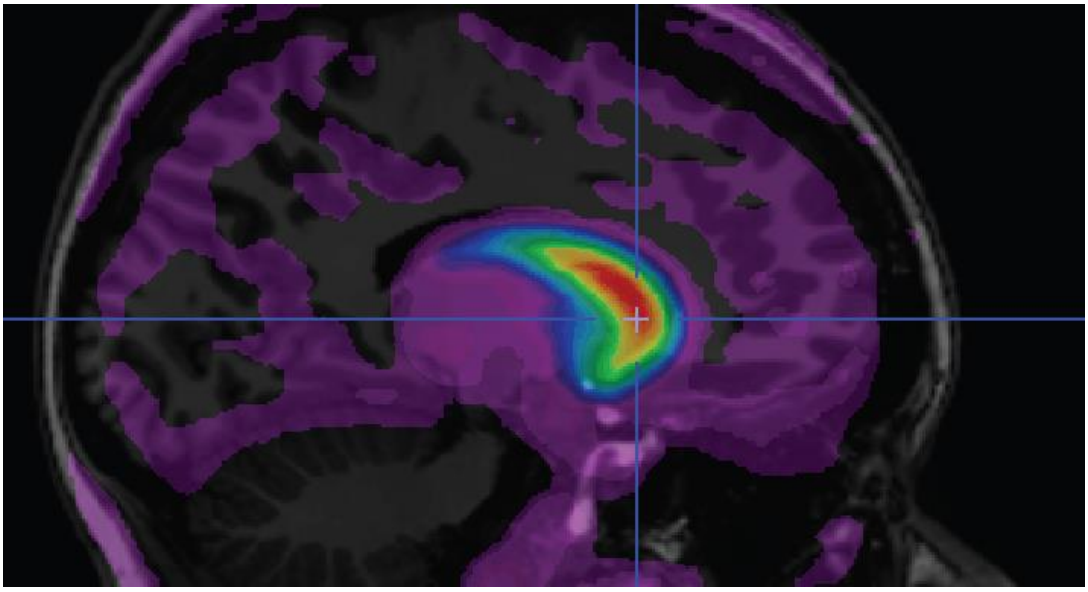

18F-Fallypride PET image. Fallypride measures dopamine D2 receptor availability. Data collected at Vanderbilt University Medical Center.

What can PET teach use about psychiatry and potential pharmacological targets?

Positron Emission Tomography (PET) is a technique used to image a variety of biological processes in living animals, including humans. PET has been around since the 1960s and involves imaging the location and amount of a radiotracer (radioactively-tagged compound) in the body. Most PET radiotracers contain C-11, F-18, or O-15 radioactive isotopes. These isotopes release positrons (which are the antiparticle of the electron) which, when they interact with nearby electrons in the body produce an annihilation event leading to 2 gamma ray photons being emitted at 180 degrees. The PET scanner "counts" these gamma ray events and ultimately reconstructs the image that produced the events by projecting the gamma ray counts back into the body part being imaged. These PET images give quantifiable data regarding the amount of tracer that accumulates in a particular area over time.

Brain PET is a particularly powerful technique in that we can use radiotracers that allow us to investigate brain metabolism, neurotransmitter receptors (dopamine or opioid, among others), neurotransmitter synthesis, and the presence of beta-amyloid plaques (often present in Alzheimer's disease). With these compounds we gain a better understanding of individual differences that may be useful as markers of disease state or risk for developing a particular disease. For example, dopamine PET techniques have demonstrated reduced D2 dopamine receptor levels in drug addiction and increased dopamine synthesis in schizophrenia.

Beyond a better mechanistic understanding of psychiatric disorders, PET can also be used to test a pharmacological compound's effectiveness at binding to specific targets in the brain. By observing how your targeted compound competes for receptor binding with

a particular radiotracer for dopamine D2 receptors, for example, you can determine its specificity as well as the degree to which its occupancy of the receptor relates to a clinical outcome of interest. Kegeles et al in 2008, referenced above, found that D2 receptor occupancy was related to the degree of positive symptoms reduction in schizophrenics being treated with a drug (Abilify) that is now widely available and prescribed. This study as well as others demonstrate the power of PET imaging in drug development. It is exciting to see groups in the UK and US (MNI, now a division of invicro) trying to use PET to advance such development and I hope we see more of this type of work in the future.

PET is a powerful technique whose potential is finally being realized by the pharmaceutical industry. Hopefully it will be used to improve the specificity and effectiveness of new compounds being developed today.