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Term paper : Use of PET and SPECT in Substance Abuse Research

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Use of PET and SPECT in Substance Abuse Research

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Abstract -
SPECT (single photon emission computed tomography) and PET (positron emission tomography) have been increasingly useful imaging techniques in the study of human psychopharmacology over the last two decades. Abusing populations can be researched several times after abstinence begins to learn more about the brain's neurochemical and physiological adjustments throughout recovery. Multiple positron labelled radiotracers can be used to study individual human participants in order to examine more than one aspect of brain activity. PET and SPECT have contributed significantly to our knowledge of many elements of the pharmacokinetics and pharmacodynamics of addictive substances, as well as pharmacological mechanisms, drug combinations (e.g. cocaine, opioids), and drug toxicities.They've also been used to investigate the symptoms of medicines on demographics of active drug users and healthy controls, as well as to assess the neurochemical repercussions of potential drug misuse treatments. PET in combination with neuropsychological testing of patients has shown to be a particularly effective technique for correlating imaging data with distinctively human features of drug effects, such as euphoria and yearning.

Introduction -

In spite of the massive public health problem associated with drug abuse, there are no completely effective treatments. This is partly due to a relatively poor understanding of the neurochemical changes that drugs of abuse produce on the human brain and the relationship of these changes to their behavioral and addictive properties. With the development of modern imaging technologies and a variety of labeled drugs and radiotracers, it has now become possible to visualize and quantify many aspects of drug pharmacokinetics and pharmacodynamics directly in the human brain and to relate these parameters to the behavioral and toxic properties of drugs. SPECT scans of substance abusers have demonstrated many abnormalities in brain areas known to be involved in behavior, such as the frontal and temporal lobes. On brain SPECT images, there are some similarities as well as differences in the damage we see caused by various substances of abuse. The most common similarity is that the brain has an overall toxic look to it; the SPECT studies look less active, more shriveled, less healthy overall and have a scalloping effect – a wavy, rough sea-like appearance on

the brain's surface. This pattern is also seen in patients who have been exposed to toxic fumes or have had oxygen deprivation. Normal brain patterns, on the other hand, show smooth activity across the cortical surface.

Single Photon Emission Computed Tomography (SPECT) –

A single photon emission computed tomography (SPECT) scan is an imaging test that shows how blood flows to tissues and organs. It may be used to help diagnose seizures, stroke, stress fractures, infections, and tumors in the spine. SPECT is a nuclear imaging scan that integrates computed tomography (CT) and a radioactive tracer. The tracer is what allows doctors to see how blood flows to tissues and organs. Before the SPECT scan, a tracer is injected into your bloodstream. The tracer is radiolabeled, meaning it emits gamma rays that can be detected by the CT scanner. The computer collects the information emitted by the gamma rays and displays it on the CT cross-sections. These cross-sections can be added back together to form a 3D image of your brain.

Fig : 1 - SPECT Scan

The radioisotopes typically used in SPECT to label tracers are iodine-123, technetium-99m, xenon-133, thallium-201, and fluorine-18. These radioactive forms of natural elements will pass through your body and be detected by the scanner. Various drugs and other chemicals can be labeled with these isotopes. The type of tracer used depends on what your doctor wants to measure. For example, if your doctor is looking at a tumor, he or she might use radiolabled glucose (FDG) and watch how it is metabolized by the tumor.

Positron emission tomography scan (PET Scan) -

A positron emission tomography (PET) scan is an imaging test that can help reveal the metabolic or biochemical function of your tissues and organs. The PET scan uses a radioactive drug (tracer) to show both normal and abnormal metabolic activity. A PET scan can often detect the abnormal metabolism of the tracer in diseases before the disease shows up on other imaging tests, such as computerized tomography (CT) and magnetic resonance imaging (MRI).

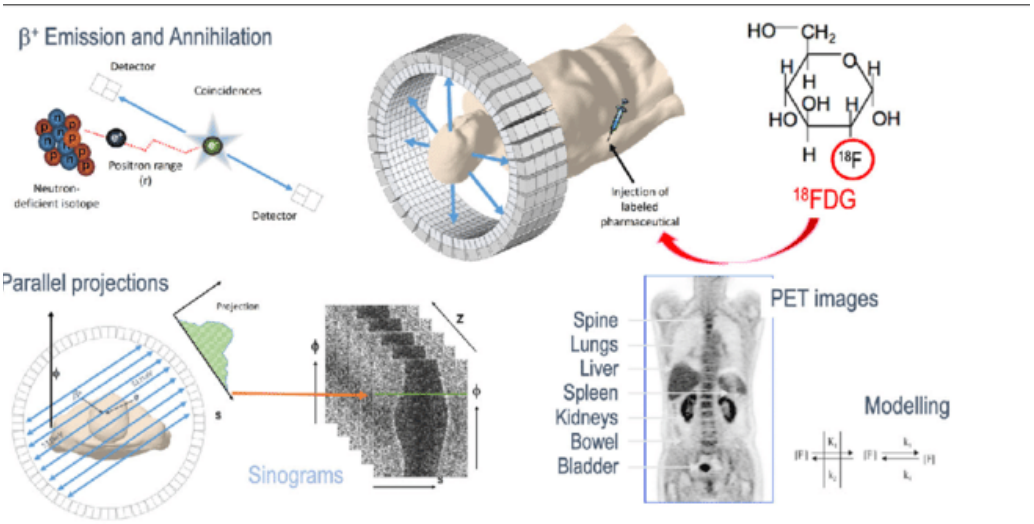

Fig : 2 - PET Scan and components it uses while working

The tracer is most often injected into a vein within your hand or arm. The tracer will then collect into areas of your body that have higher levels of metabolic or biochemical activity, which often pinpoints the location of the disease. The PET images are typically combined with CT or MRI and are called PET-CT or PET-MRI scans.

PET works by using a scanning device (a machine with a large hole at its center) to detect photons (subatomic particles) emitted by a radionuclide in the organ or tissue being examined. The radionuclides used in PET scans are made by attaching a radioactive atom to chemical substances that are used naturally by the particular organ or tissue during its metabolic process. For example, in PET scans of the brain, a radioactive atom is applied to glucose (blood sugar) to create a radionuclide called fluorodeoxyglucose (FDG), because the brain uses glucose for its metabolism. FDG is widely used in PET scanning. Other substances may be used for PET scanning, depending on the purpose of the scan. If blood flow and perfusion of an organ or

tissue is of interest, the radionuclide may be a type of radioactive oxygen, carbon, nitrogen, or gallium.

Imaging Study	Radioligand	Target
PET	[^{11}C] raclopride	D2 Dopamine receptor
	[^{11}C] cocaine	Dopamine transporter
	[^{11}C] methylphenidate	
	[^{11}C] McN5652	Serotonin transporter
	[^{18}F] fluorodeoxyglucose	Brain glucose metabolism
	[^{15}O] H2O	Cerebral blood flow
SPECT	^{99m}Tc-HMPAO	
	[^{123}I] Iodobenzamide	D2/D3 dopamine receptors

Table 1 : Most Common Radiotracers Used in Drug Abuse Research and its Targets

Neuropharmacological characteristics such as accessible receptors, uptake sites, enzymes, and neurotransmitter turnover are measured using PET and SPECT. A suitable ligand to identify the subject of interest is required, yet such ligands do not exist for many neurotransmitter systems. The impacts of medications on the brain (so-called pharmacoMRI) may be measured using fMRI, but only indirectly through blood flow. The use of this method to investigate addiction is still in its early stages.

Specific Absuses -:

1. **<u>Cocaine -</u>**

Cocaine is a tropane alkaloid and stimulant substance derived principally from the leaves of Erythroxylum coca and Erythroxylum novogranatense, two coca species endemic to South America. It is among the most addictions on the market. Changes in the central and peripheral vasculature are caused by its sympathomimetic effect. Cocaine raises extracellular DA via reducing DA absorption by blocking dopamine transporters (DAT). This rise in extracellular DA has traditionally been linked to drug reinforcing effects. To put it another way, the medication floods the areas of your brain that govern pleasure with dopamine, a naturally chemical transmitter in your body. The accumulation generates a high, which is characterised by heightened sensations of energy and alertness.

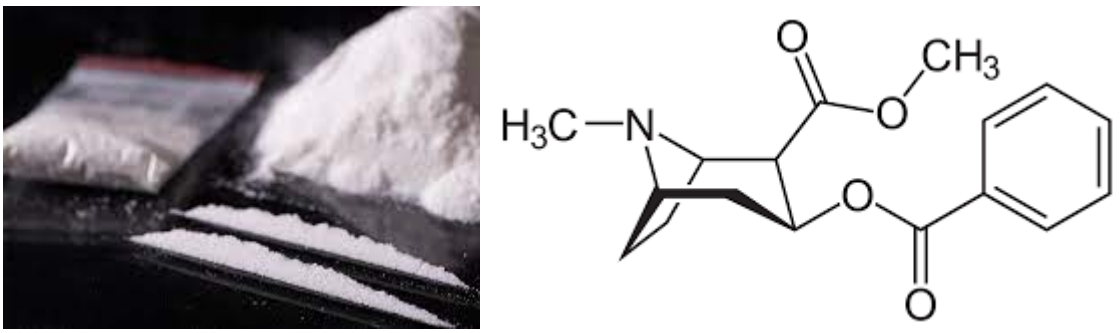

Fig : 3 - Cocaine and it's molecular structure

Because anticipation can intensify the effects of the drug, Volkow et al. [13] looked explored how it affected cocaine abusers' brain metabolism when they expected to receive a substance comparable to cocaine — methylphenidate — vs when they didn't (i.e. told they were getting placebo). Individuals who anticipated and got methylphenidate had more activity in the cerebellum and thalamus, while those who were not anticipating the medication had more engagement in the orbitofrontal cortex. Variations in thalamic metabolism were also linked to self-reports of 'high,' which were 50 percent higher when individuals expected the medication vs when they didn't. Dopaminergic projections are received by the thalamus, which has reciprocal connections with the frontal cortex and striatum.

In chronic cocaine addicts, positron emission tomography [18F]-fluorodeoxyglucose investigations revealed increased metabolism in the cerebellum and reduced metabolism in the frontal and temporal cerebral cortexes (Fig. 4), both of which have been linked to DA D2 availability.

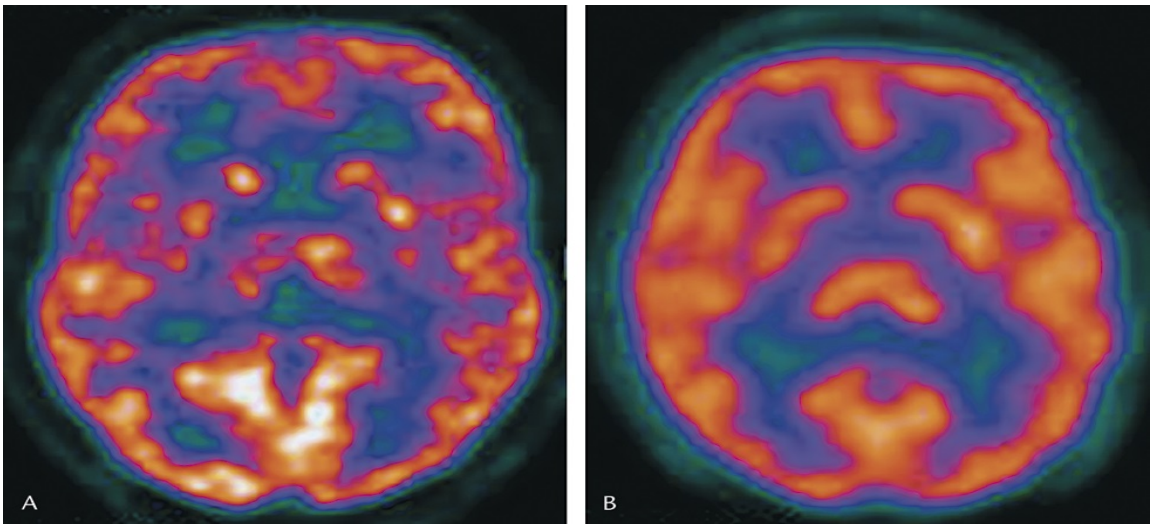

Fig : 4 - A) FDG PET scan of a patient with history of cocaine abuse demonstrating an heterogenous radiotracer concentration in the cortex related to brain atrophy. (B) FDG PET scan of a normal patient.

2. Opiates -

Opioids affect the body's natural opioid network, which controls hunger, emotions, and stress response, among other things. Opioids also disinhibit the ventrotegmental DA cells, causing an increase in their firing rate and, as a result, a rise in dopamine levels. Opioids are a class of medications that function by engaging with opioid receptors in your cells to relieve pain. Opioids can be extracted from the poppy plant, such as morphine (Kadian, Ms Contin, and others), or produced in a lab, such as fentanyl (Actiq, Duragesic, others). When opioid drugs pass through your bloodstream and bind to opioid receptors in your brain cells, the cells send out signals that reduce your pain perception while increasing your pleasure.

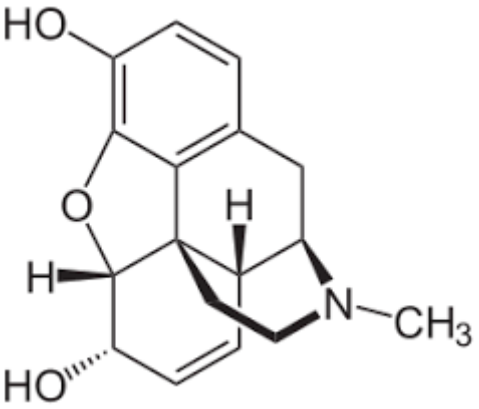

Fig : 5 - Opioids and it's molecular structure

[15O]H2O In the usage of heroin and other opiates, PET has been used to assess cerebral blood flow (CBF). The brain stem, periaqueductal grey matter, and ventrotegmental area, as well as the cingulate gyrus, orbitofrontal cortex, and caudate nuclei, all show an increase in rCBF. [11C]-carfentanil and [11C]-diprenorphine are two radiotracers that have been utilised to imaging the opioid system using PET. These have aided in the knowledge of the role of mu opioid receptors, which are associated to euphoria and are enhanced in opioid abusers, as well as kappa opioid receptor in opioid misuse and pain pathophysiology. This has contributed in the creation of drugs to treat substance misuse by reducing the psychologic and physiological impacts.

Using morphine sulphate and [18F] fluorodeoxyglucose PET, the effect of opioids on cerebral metabolism was investigated, revealing a worldwide 10% reduction in cerebral metabolism rate of glucose (CMRglu), as well as localised reductions in the frontal and temporal lobes and cerebellum.

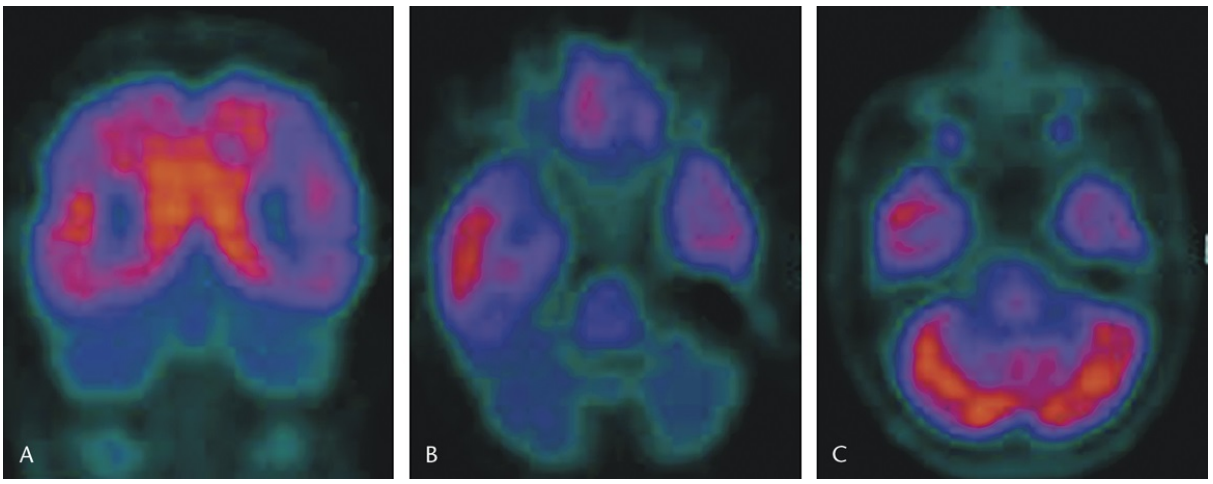

Fig : 6 - (A) and (B) coronal and axial FDG PET scan in a 50-year-old heroin abuser showing a bilateral reduced cerebellar gray matter uptake. (C) Normal axial FDG PET scan.

3. Cannabis (Marijuana)

Cannabis, sometimes referred to as marijuana, is a psychoactive substance derived from the Cannabis plant. The cannabis plant, which is native to Central and South Asia, has long been used as a pleasure and entheogenic substance, as well as in numerous herbal healers. The major psychoactive component of cannabis is tetrahydrocannabinol (THC), which is one of 483 recognised chemicals in the plant, including at least 65 additional cannabinoids, notably cannabidiol (CBD). Cannabis may be used in a variety of ways, including smoking, vaporising, cooking with it, and extracting it. Euphoria, changed states of mind and perception of time, trouble concentrating, reduced short-term memory, impaired bodily motion (balance and fine psychomotor control), relaxation, and an increase in hunger are some of the mental and physical effects of cannabis.

Fig : 7 - Cannabis Leaves

When chronic marijuana users are drunk, their CBF is increased in the orbitofrontal cortex, prefrontal cortex, and basal ganglia using SPECT and PET. When compared to normal people, glucose metabolism was lower at baseline or in non-chronic users. Cerebellar metabolism is also higher in these patients, which has been linked to the higher densities of cannabinoid receptors identified in this location.

Conclusion -

Neuroimaging studies have greatly aided our understanding of the consequences of drug abuse on the brain and have demonstrated the involvement of a wide variety of brain areas. Future uses will rely on technological advancements such as increased resolution, shorter acquisition times, and the creation of neurotransmitter-sensitive PET and SPECT tracers. Furthermore, the application of these tools to comprehend the interaction of the environment and genes with brain activation in addictions is still in its early stages. Furthermore, these neuroimaging modalities can be utilised to track illness development and measure treatment response to medications and other therapeutic treatments.

Finally, PET and SPECT imaging may lead to more study focused on the brain areas that have been proven to be the most significantly implicated by imaging. The effects of therapy might be studied, as evidenced by differences in imaging results between postintervention PET and SPECT tests. Additional study might also assist identify, in a more unbiased way, which treatment medicines or procedures can be employed to avoid further neuronal degeneration in addicted people. Additional studies using PET and SPECT imaging might reveal novel therapeutic intervention paths.

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