Chapter 5 – Clinical applications of PET/CT in neurology

5.3 Psychiatry
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Introduction

Neuroimaging in psychiatry has been used to assess functional, neurochemical and structural patterns related to specific disorders, to evaluate new molecules as therapeutic agents and to foresee individual response to treatment. In psychiatric studies, comorbidity is a critical issue since the co-occurrence of different pathological dimensions might impact on the neurobiological patterns, causing the neuroimaging findings to be unspecific. Furthermore, macroscopic changes have seldom been described since most psychiatric diseases show changes at the molecular level. All this results, for all forms of anxiety disorder, in a diagnostic accuracy far below that reported in neurodegenerative disorders. In this respect the diagnostic approach to the various mental disorders included in DSM-IV Axis I (major mental and learning disorders) needs specific knowledge in order to adopt the correct strategies for patient selection as well as advanced radiochemical and statistical methodologies. In most of the mental disorders included in DSM-IV Axis I, CBF, metabolism and transporter/receptor patterns have been investigated but only in some of them has a general consensus been reached.

Major depression

Major depression (MD) is a common primary idiopathic condition characterised by one or more major depressive episodes of persistently low mood, dysregulated sleep, appetite and weight, anhedonia, cognitive impairment, and suicidality not due to a medical condition, medication, abused substance or psychosis. MD is estimated to rival virtually every other known medical illness in burden of disease morbidity early in this millennium since it is estimated to affect, on a life-time basis, up to a quarter (26%) of the population. The neural networks modulating emotional expression seem to be implicated in the pathophysiology of MD, and this is in particularly true of the medial prefrontal cortex, amygdala, hippocampus and basal ganglia, as reported by several PET studies. Serotonin 1A receptor (5-HT1AR) function appears to be abnormal in MD but disagreement still exists regarding the presence and direction of binding abnormalities [1]. An important use of PET in MD is the study and follow-up of antidepressant effects on monoamine receptor occupancy [2].

Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) is an anxiety disorder following major psychological trauma reported to affect between 4% and 8% of the general population. It is defined by the coexistence of three clusters of trauma-related symptoms: re-experiencing, avoidance and hyperarousal. Neural correlates of PTSD have been investigated by means of different research paradigms such as symptom provocation, cognitive activation and functional connectivity. Functional studies by PET have consistently shown during emotional stimuli a concomitance of amygdala hyper-reactivity and a correspondingly reduced prefrontal
cortex and anterior cingulate cortex control over amygdalae. However, other structures have been consistently found to be involved in PTSD, i.e. anterior and posterior insular cortex, posterior cingulate cortex and certain portions of the temporal lobe and orbitofrontal cortex ([3]; for review see [4]). Figure 1 illustrates increased CBF in PTSD as demonstrated by $^{99m}$Tc-HMPAO SPECT imaging analysed by SPM2.

Attention deficit hyperactivity disorder
Attention deficit hyperactivity disorder (ADHD) is a multifactorial and clinically heterogeneous neurobehavioural disorder characterised by symptoms of hyperactivity, inattention and impulsivity. It is suggested to be the most common chronic undiagnosed psychiatric disorder in adults and its prevalence in adults is estimated to be about 4%. Comorbidity with at least one other psychiatric disorder occurs in 87% of adult ADHD subjects. Neuroanatomical and neurobiological data underscore alterations in dopamine/noradrenaline-modulated fronto-striatal-cerebellar circuits. Owing to the high catecholamine concentration in these sensitive regions, both dopamine transporters and receptor ligands have often been used in ADHD studies [5] and the effect of stimulants, mostly methylphenidate, investigated. Moreover deficits in CBF and metabolism have been reported in both adolescents and adults with ADHD (for review see [6]).

Autism spectrum disorders
Autism spectrum disorders (ASDs) are defined on the clinical basis by impairment in social interaction, impairment in verbal and non-verbal communication and repetitive or stereotypical behaviours. They affect almost 1% of the general population and have shown an impressive increase in prevalence since the early 1990s, probably attributable to the better awareness of the disease. Structural findings support the hypothesis of anomalous perinatal processes of neurogenesis and neuronal
maturation [7]. Regional CBF or metabolism abnormalities have been found in the cerebellum, limbic system, frontal and temporal cortices, corpus callosum and basal ganglia even though specific patterns for ASD have not yet been identified [8]. Furthermore, a growing body of evidence suggests weaker functional connectivity, especially in the default network, often associated with symptom severity.

Conclusion
Neuroimaging in psychiatric disorders will help to provide a better understanding of the underlying pathophysiology, to assess the neurobiology of treatment outcome and to demonstrate the neuroanatomical, functional and chemical profiles associated with specific endophenotypes. It will also contribute in disclosing the neurobiology of the specific symptoms underlying psychiatric disorders and in progressing towards a more suitable dimensional approach.
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References


