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Review

Molecular imaging of striatal dopamine transporters in major depression—A meta-analysis

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ABSTRACT

Background: Increasing studies have revealed the dopamine transporter (DAT) availability altered in striatum associated with major depression. However, the results remain inconsistent.
Methods: To assess the alteration of striatal DAT availability in major depression, we performed a meta-analysis based on 12 case-control molecular imaging studies, including a total of 209 depressed patients and 314 healthy controls. Hedges' *g* and corresponding 95% confidence intervals (CIs) for striatal DAT availability in major depression compared with controls were estimated.
Results: Our meta-analysis revealed no evidence for the alteration of striatal DAT availability in major depression (Hedges' $g=0.09$, CI 95% from -0.43 to 0.61, $P=0.73$). Meta-regression analyses suggested that there were no moderating effects for age, gender, year of publication, sample size, medication exposures and severity of depression on the hedges'*g* values for striatal DAT availability.
Limitations: The results should be treated with caution because of the significant heterogeneity and the potential interference of confounding factors in this meta-analysis.
Conclusions: Our results showed no altered striatal DAT availability in major depression and indicated that striatal DAT may not implicated in the pathophysiology of major depression.

Contents

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1. Introduction

Major depressive disorder (MDD) is a common psychiatric disorder with an estimated prevalence of 20% in lifespan (Ustun et al., 2004). It is characterized by a pervasive, persistent depressed mood and a loss of interest or pleasure. Accumulating evidence suggests that MDD can increase the rate of smoking, substance misuse, obesity and suicide apart from causing health impairments. Although great advances have been made in epidemiology and neurobiology, the underlying pathophysiology of the illness remains unclear, partly due to the clinical heterogeneity and diverse causal factors.

The monoamine hypothesis suggests that major depression might be a result from the dysregulation of monoaminergic neurotransmitters such as dopamine, serotonin and norepinephrine in the central nervous system. Dopamine is the most abundant monoamine neurotransmitter in the brain and plays a critical role in the regulation of emotions, motivation, cognition, reward circuits and reinforcement behavior (Nieoullon and Coquerel, 2003; Perkins et al., 2008; Wise, 2004). The dopaminergic system originates in the deep brain and projects to over almost the entire brain, modulating various functions in specific brain areas. Multiple lines of evidence have supported the hypothesis that dopaminergic neurotransmitter was deficient in patients with major depression (Dunlop and Nemeroff, 2007; John Mann and Malone, 1997; Lambert et al., 2000; Lu et al., 1986; Roy et al., 1992; Ruhe et al., 2007).

Dopamine transporter, located at the membrane of presynaptic terminals, acts as crucial roles in regulating the dopamine intensity and the duration of dopaminergic neurotransmission in the synaptic cleft by absorbing the dopamine molecules from the synaptic cleft into presynaptic neuron (Fig. 1). The dysfunctional DAT can cause dopaminergic abnormalities that have been supposed to implicate in the pathologies of several psychiatric disorders. Although it is difficult to measure the dopaminergic function directly, recent evidence indicated that the availability of DAT may reflect the general status of dopaminergic function in brain (Jaber et al., 1997; Meyer, 2007). Previous postmortem studies reported that DAT density reduced in brain in major depression (Klimek et al., 2002; Rao et al., 2012). However, postmortem studies are limited to measure the availability of DAT in living patients and are potentially biased by the effects of antidepressants, postmortem tissue's quality and agonal events. Recent advance in neuroimaging using single-photon emission computed tomography (SPECT) or positron emission tomography (PET) enables the investigation of dopaminergic transporter in vivo. Many neuroimaging studies have been performed to measure the availability of DAT in patients with major depression comparing with healthy controls, but results were contradictory. There have been several papers reviewed the DAT in major depression (Camardese et al., 2014; Savitz and Drevets, 2013). But, to our knowledge, no meta-analysis has been performed to quantify the magnitude of DAT availability in major depression.

In the current meta-analysis, we synthesized available molecular imaging (PET, SPECT) studies to calculate the pooled effect-size estimates on differences in availabilities of striatal DAT between MDD and healthy controls. We focus on striatum in brain, partly because of the striatal dopaminergic pathway supposed to be associated with mood, and partly because the striatum has the highest density of DAT in brain and is reliable for imaging DAT measurement. To test the potential effect of confounding variables, subgroup analyses (radiotracers) and meta-regression analyses (age, gender, published years, sample size, and medication exposure) were performed.

2. Methods

We carried out a meta-analysis following to the guidelines that are recommended by PRISMA (Preferred Reporting Items for

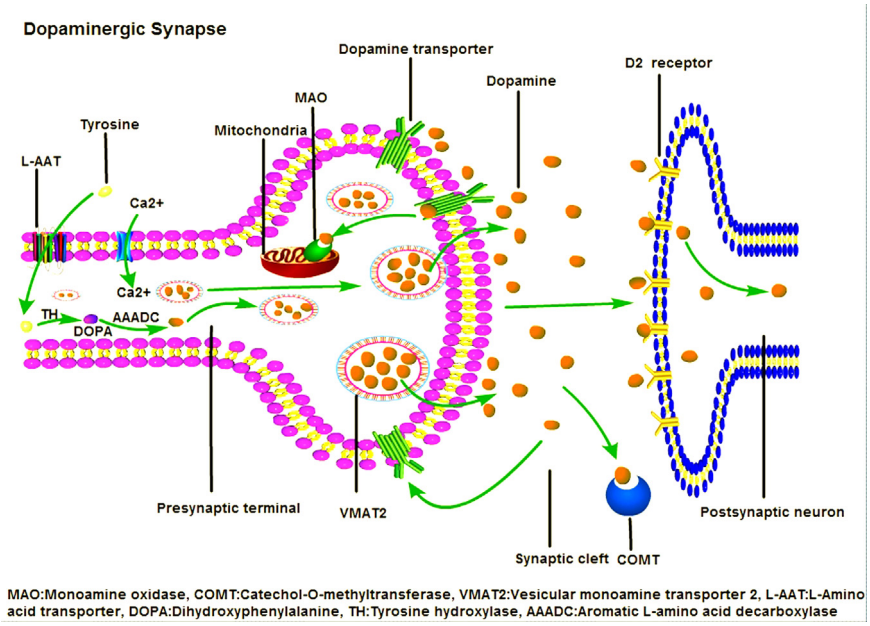

Fig. 1. Schematic diagram of dopaminergic synapse.