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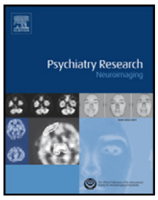

Extraction of prefronto-amygdalar pathways by combining probability maps

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ABSTRACT

Many recent studies reported altered functional connectivity within the frontolimbic circuitry in a wide range of neuropsychiatric disorders. However, functional connectivity must rely on structural connections. In this study we applied a novel probabilistic fiber tracking method to assess the structural connectivity between the amygdala and different prefrontal brain regions in vivo. Twenty healthy subjects were investigated with diffusion tensor imaging. Probabilistic fiber tracking was started from the amygdala and different prefrontal brain regions. Resulting probability maps were combined using an extended multiplication of probabilistic maps to identify the most probable anatomical pathways connecting these structures. We found one ventral pathway through the uncinate fascicle, connecting the amygdala and the medial and lateral orbitofrontal cortices. In addition to this ventral pathway, we depicted distinct dorsal pathways (medial and lateral), which connect the amygdala with the anterior cingulate cortex and the dorsolateral prefrontal cortex. The dorso-medial pathway proceeds through the inferior thalamic peduncle, while the dorsolateral pathway travels through the external capsule. We believe that our approach provides a promising tool to assess the integrity of specific structural connections in patients with neuropsychiatric disorders.

1. Introduction

A number of recent studies have investigated functionally connected neural networks in neuropsychiatric disorders across different frontolimbic brain areas in order to not only analyze discrete brain subareas but also distributed functionally connected neural networks (Heinz et al., 2005; Pezawas et al., 2005; Castellanos et al., 2008). For example, in a recent functional imaging study, failure of inhibitory function in the medial orbitofrontal cortex and the subgenual anterior cingulate and hyperactivity of the amygdala in turn were demonstrated in patients with borderline personality disorder (Silbersweig et al., 2007). However, functional connectivity must rely on structural connections. Therefore, there has been increasing interest in the structural organization of the prefrontal and limbic brain. From a neuropsychiatric point of view, it would be of great importance to identify the structural connectivity between the main relay stations of these frontolimbic pathways since altered functional connectivity (Heinz et al., 2005; Pezawas et al., 2005) and functional disturbances within these networks should be reflected by structural alterations.

At present, fiber tracking based on diffusion tensor imaging (DTI) is the only existing technology enabling reconstructions of neuronal fibers in vivo and offers a unique insight into human brain anatomy. So far, mostly association pathways have been visualized, presenting impressive results (e.g. Basser et al., 1994; Makris et al., 1997; Mori and van Zijl, 2002; Catani et al., 2002). In many studies these methods could detect and characterize white matter abnormalities. For example, altered structural connectivity of the uncinate fascicle was found in schizophrenia (e.g. Kubicki et al., 2007; Rosenberger et al., 2008; Sussmann et al., 2009), bipolar disorder (Houenou et al., 2007; Sussmann et al., 2009) or temporal lobe epilepsy (McDonald et al., 2008). A novel development in DTI fiber tracking is that by combining probability maps the most probable anatomical pathway(s) connecting two regions of interest can be extracted (Kreher et al., 2008). So far, this method has

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