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Development of the uncinate fasciculus: Implications for theory and developmental disorders

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ABSTRACT

The uncinate fasciculus (UF) is a long-range white matter tract that connects limbic regions in the temporal lobe to the frontal lobe. The UF is one of the latest developing tracts, and continues maturing into the third decade of life. As such, individual differences in the maturational profile of the UF may serve to explain differences in behavior. Indeed, atypical macrostructure and microstructure of the UF have been reported in numerous studies of individuals with developmental and psychiatric disorders such as social deprivation and maltreatment, autism spectrum disorders, conduct disorder, risk taking, and substance abuse. The present review evaluates what we currently know about the UF's developmental trajectory and reviews the literature relating UF abnormalities to specific disorders. Additionally, we take a dimensional approach and critically examine symptoms and behavioral impairments that have been demonstrated to cluster with UF aberrations, in an effort to relate these impairments to our speculations regarding the functionality of the UF. We suggest that developmental disorders with core problems relating to memory retrieval, reward and valuation computation, and impulsive decision making may be linked to aberrations in uncinate microstructure.

Contents

The human brain follows a distinct spatial and temporal pattern of maturation that begins with phylogenetically older posterior and inferior regions and then progressively extends to more anterior and superior regions (for reviews, see Durston et al., 2001; Lenroot & Giedd, 2006; Toga et al., 2006). Postmortem (Huttenlocher et al., 1994; Yakovlel & Lecours, 1967), MRI (Courchesne et al., 2000; Durston et al., 2001; Giedd et al., 1999a; Giedd et al., 1999b; Gogtay et al., 2004; Good et al., 2001; Matsuzawa et al., 2001; Paus et al., 1999; Sowell et al., 2003), and diffusion tensor imaging (DTI) studies (Barnea-Goraly et al., 2005; Bava et al., 2010; Giorgio et al., 2008; Hasan et al., 2007; Lebel & Beaulieu, 2011; Lebel et al., 2012; McKinstry et al., 2002; Mukherjee & McKinstry, 2006; Mukherjee et al., 2001; Schmithorst & Yuan, 2010; Schneider et al., 2004; Snook et al., 2007; Yap et al., 2013) suggest that concurrent changes in gray and white matter are two important events that follow distinct

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developmental trajectories that significantly contribute to brain maturation.

The increase in global gray matter volume during development follows an inverted U-shaped curve that increases and peaks during adolescence and then decreases until early adulthood, whereas global white matter increases steadily throughout childhood into adulthood (Giedd et al., 1999a). If maturational changes are examined over the course of the entire lifespan, global white matter volume also follows an inverted U-shaped trajectory, with white matter volume reaching its peak around 40 years of age (Hasan et al., 2007; Lebel et al., 2012). It is believed that the function of cortical regions is based on the intrinsic properties and extrinsic pattern of white matter input and output and that the information transmission properties of a given white matter tract can be predicted by the functions of the cortical regions it connects (Passingham et al., 2002; Van Essen & Maunsell, 1983). Although the function of the *uncinate fasciculus* (UF) is still largely unclear, its location and connectivity often associate it with the limbic system and its functions (e.g., emotion, episodic memory, etc.), making it a likely candidate for disruption in disorders affecting personality, emotion, and episodic memory. The extended development of this white matter tract into the third decade of life might also make it more susceptible to disruptions in function and could help explain why the UF has been implicated in several developmental and psychiatric disorders.

We previously reviewed the human adult and non-human primate literature on the UF (Von Der Heide et al., 2013). The purpose of the present literature review is to integrate current knowledge about the UF's developmental trajectory with the relevant literature on developmental disorders, while placing them in the theoretical context of our findings on the adult UF. We believe that this review will be of interest to both clinicians and cognitive scientists, and we aim to link the UF to clinical disorders, as well as to normal cognition, as we believe that one informs the other.

1. Anatomy and maturation of the uncinate fasciculus

We described the anatomy of the uncinate fasciculus previously (Von Der Heide et al., 2013). In brief, it is a long-range association pathway that creates a monosynaptic pathway between the anterior temporal lobes (BA 38 including perirhinal cortex and portions of the anterior parahippocampal gyrus) and amygdala to the lateral orbitofrontal cortex (OFC; BA 11, 47/12) and BA 10. It has a distinctive hook shape, arcing around the Sylvian fissure into the frontal lobe (see Fig. 1; Schmahmann & Pandya, 2006; Thiebaut de Schotten et al., 2012). It is frequently damaged in epilepsy resection surgery, as well as blunt-force trauma affecting the frontal lobes.

The UF is one of the last white matter tracts to reach its maturational peak, with its developmental time course extending throughout adolescence, young adulthood, and peaking beyond the age of 30 (see Fig. 2; Lebel et al., 2012; Lebel et al., 2008). Although the basic characteristics of UF macrostructure (e.g., volume, length, shape) have been reported in adult studies (Hasan et al., 2009; Malykhin et al., 2008; Taoka et al., 2006; Wakana et al., 2007), little is known about the trajectories of these characteristics across development. Until recently, when developmental DTI studies began to fill in gaps of knowledge, relatively little has also been known about maturational changes in the microstructural characteristics of the UF.

Recent developmental DTI studies report that from childhood to adulthood, fractional anisotropy (FA) values, which are thought to reflect myelination, white matter organization, and the density

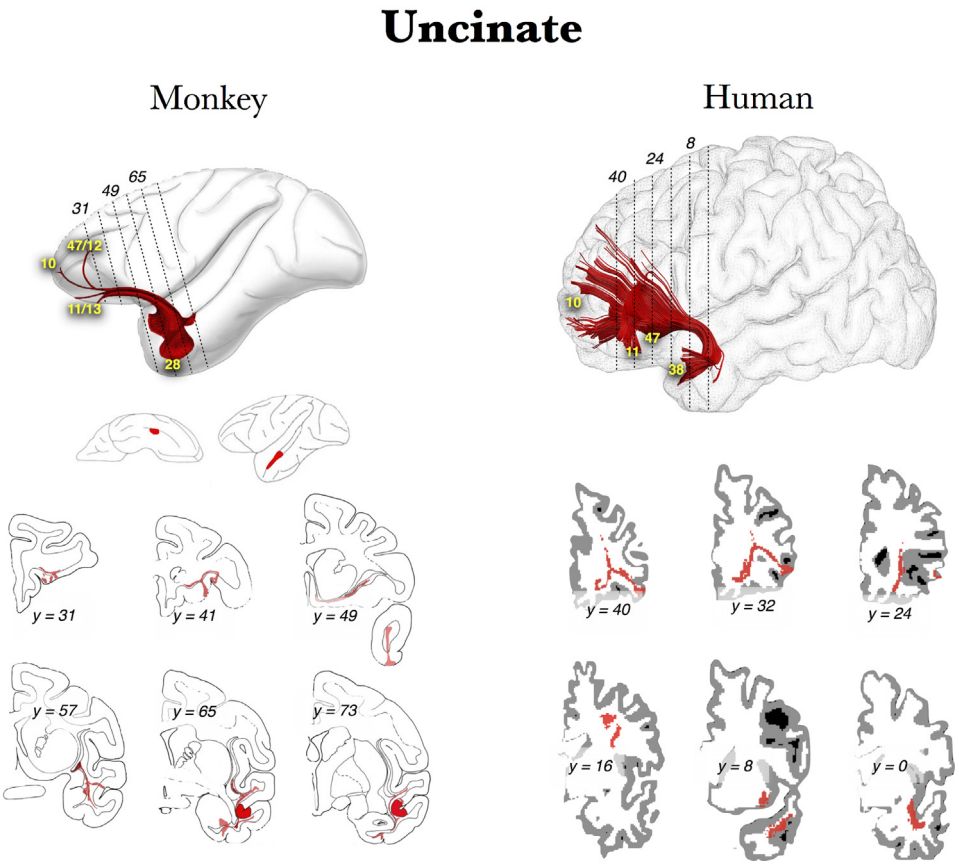

Fig. 1. Reconstructions of the uncinate fasciculus: comparison between post-mortem axonal tracing in monkey and human in vivo Spherical Deconvolution (SD) tractography suggests simian-human similarities (Thiebaut de Schotten et al., 2012). Used with permission.