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## THE UNCINATE FASCICULUS AND EXTRAVERSION IN SCHIZOTYPAL PERSONALITY DISORDER: A DIFFUSION TENSOR IMAGING STUDY

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The uncinate fasciculus (UF) is the most prominent white matter tract connecting frontal and temporal brain regions, and is altered in schizotypal personality disorder (SPD) (Nakamura et al, 2005). SPD is also associated with elevated neuroticism and reduced extraversion and agreeableness (Gurrera et al, 2005a). Since brain regions connected by the UF play important roles in personality function, we tested the hypothesis that UF white matter integrity and personality dimensions are interrelated in SPD.

Eleven neuroleptic-naive men with SPD and eight psychiatrically healthy men were recruited from the community for magnetic resonance studies of SPD (Nakamura et al, 2005). Subjects were included in the present analysis if they also completed a personality questionnaire (NEO Five Factor Inventory: Costa and McCrae, 1992).

Fiber tract coherence was measured by fractional anisotropy (FA); a higher FA index indicates greater water diffusion directionality in the fiber tract, since water diffusion is greater inside the axon than across the myelin sheath (i.e., diffusion is “anisotropic”). Line scan diffusion tensor imaging and computational measures were performed as previously described (Kubicki et al, 2002). Multiple linear regression, with right and left FA entered as independent variables, was used to evaluate the relationship between UF integrity and personality measures. Standardized regression coefficients ( $\beta$ ) are reported; probabilities are two-tailed.

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SPD and comparison groups did not differ in mean age ( $39.2 \pm 13.0$  vs.  $34.2 \pm 9.8$  years), subject or parental SES, educational level, or full scale IQ. SPD subjects had higher mean Neuroticism ( $58.7 \pm 14.6$  vs.  $39.0 \pm 6.4$ ,  $t = 3.55$ ,  $df = 17$ ,  $p = .002$ ), and lower mean Extraversion ( $43.6 \pm 13.5$  vs.  $59.7 \pm 4.9$ ,  $t = -3.20$ ,  $df = 17$ ,  $p = .005$ ) and Agreeableness ( $41.8 \pm 14.1$  vs.  $58.1 \pm 10.3$ ,  $t = -2.76$ ,  $df = 17$ ,  $p = .013$ ).

SPD subjects had significantly lower mean right FA ( $592.5 \pm 40.5$  vs.  $638.1 \pm 42.9$ ,  $t = -2.37$ ,  $df = 17$ ,  $p = .030$ ) and left FA ( $597.1 \pm 43.8$  vs.  $641.4 \pm 42.2$ ,  $t = -2.21$ ,  $df = 17$ ,  $p = .041$ ) (Figure 1A). No differences in mean diffusivity or cross-sectional area were found.

In SPD subjects, FA strongly predicted Extraversion ( $F_{[2,8]} = 16.02$ ,  $p = .002$ ), but only on the right side ( $\beta = .89$ ,  $p = .001$  vs.  $\beta = .02$ ,  $p = .883$ ). Moreover, FA weakly predicted Agreeableness in SPD subjects ( $F_{[2,8]} = 4.38$ ,  $p = .052$ ), again only on the right side ( $\beta = .58$ ,  $p = .048$  vs.  $\beta = .33$ ,  $p = .225$ ), and there was also a trend toward right FA predicting Neuroticism ( $F_{[2,8]} = 4.64$ ,  $p = .046$ ;  $\beta = -.54$ ,  $p = .061$  vs.  $\beta = -.40$ ,  $p = .139$ ). Of note, there were no significant results for comparison subjects. Figure 1B illustrates the relationship between right UF FA and Extraversion.

Personality and UF anatomy alterations in SPD resemble those found in schizophrenia (Gurrera et al, 2000; Kubicki et al, 2002), and some clinical features of schizophrenia may reflect fronto-temporal connectivity abnormalities (McGuire and Frith, 1996). Personality changes in schizophrenia may also stem from altered brain function (Gurrera et al, 2005b). The present data suggest that reduced right UF integrity contributes to reduced extraversion in SPD.

Interestingly, the UF appears to mediate auto-noetic awareness, or awareness of oneself as a continuous entity across time, which is manifested in the ability to re-experience remembered events as part of one's past (Levine et al, 1998). In unstructured situations, auto-noetic awareness supports the formulation of goals and the behavioral oversight needed to attain them (Levine et al, 1998). Thus, individual differences in auto-noetic awareness could contribute to variation in human approach-avoidance behaviors, especially in unstructured social situations where individual differences in extraversion are most evident.

This study is limited by small sample size. Exclusive reliance on a self-report personality measure is also a potential limitation, though observer-based personality measures are subject to similar biases (Ozer, 1999).

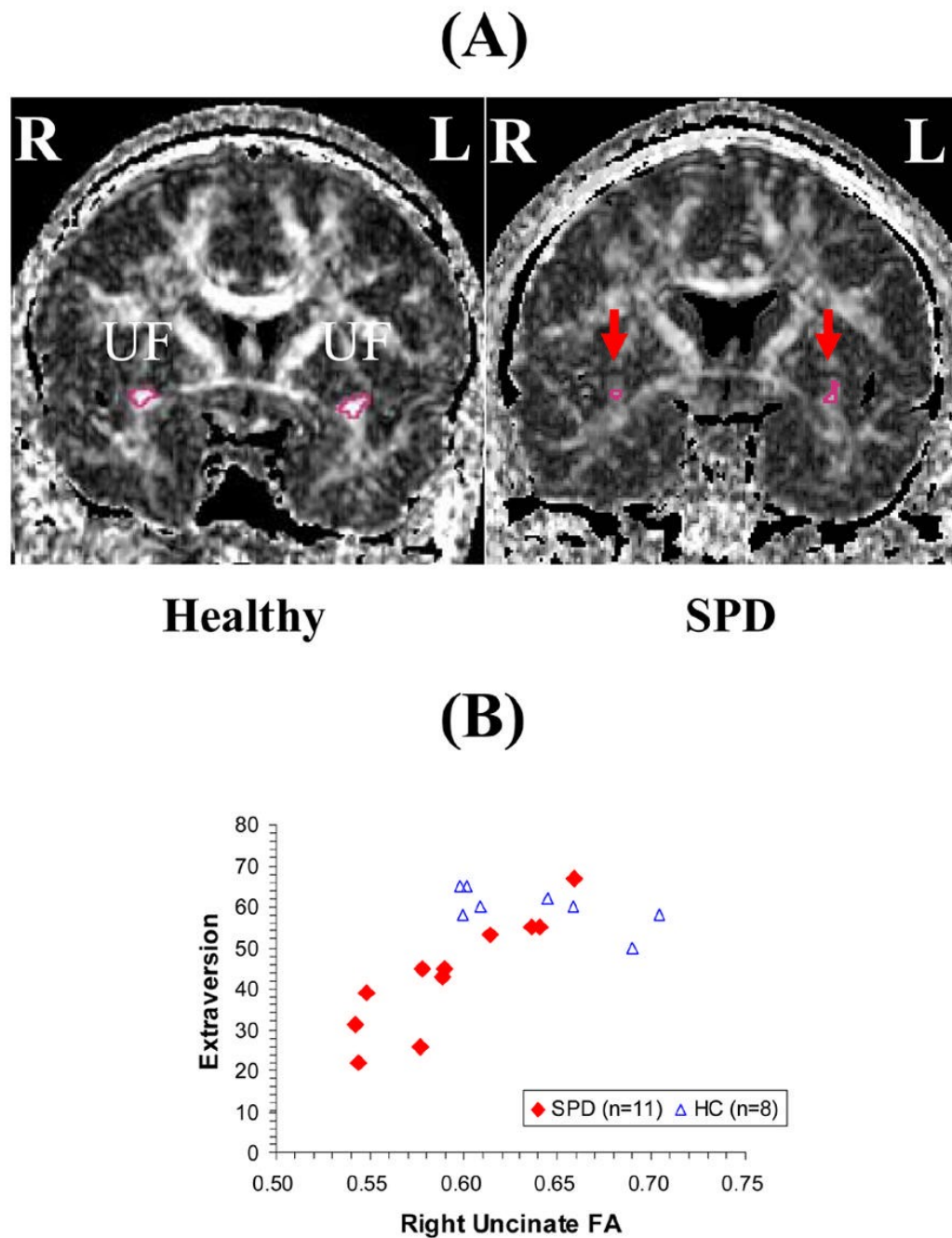
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**FIGURE 1. The Uncinate Fasciculus (UF) and Extraversion in SPD**

(A) Line-scan diffusion tensor imaging (LSDTI) produced these contrasting coronal views of uncinate fasciculi (UF) in comparison (left) and SPD (right) subjects.

(B) Graph illustrates the relationship of extraversion to right uncinate fasciculus (UF) fractional anisotropy (FA) in SPD (Pearson  $r = .89, p = .0002$ ) and comparison ( $r = -.66, p = .075$ ) subjects.