BACKGROUND
This study compared diffusion measures in the uncinate fasciculus (UF) of young, unmedicated, first episode schizophrenic patients (FESZs) to those of age-matched controls (NCs).

METHODS
Diffusion-weighted images (DWI) were acquired on a 3T GE EchoSpeed system from 17 FESZs and 17 group-matched NCs. Regions of interest (ROIs) were manually traced over the temporal pole and temporal pole in each hemisphere, and each ROI was seeded for tracks using 3D Slicer. The UF tract was isolated and FA, trace, and mode were analyzed over the whole tract.

RESULTS
No significant differences were found between NCs and FESZs for FA or mode, but a significant increase was found in trace in NCs in both hemispheres (p=0.033, left; p=0.015, right). A trend was observed for higher FA in the left uncinate fasciculus (p=0.085).

CONCLUSIONS
These findings indicate greater diffusivity of water in the uncinate fasciculus fiber tract at the first episode of schizophrenia. This suggests that some minor abnormalities are present at the onset of illness, which may worsen over time.

SCHIZOPHRENIA AND THE UNCINATE FASCICULUS
Schizophrenia has long been hypothesized to be a disorder of connectivity (Friston & Frith, 1995). Disruptions between the frontal and temporal lobes have been especially implicated (Burns, 2003). The uncinate fasciculus is the most prominent white matter tract connecting the frontal and temporal lobes of the brain (Kubicki et al., 2002; Figure 1).

DIFFUSION TENSOR IMAGING
Fractional anisotropy (Figure 2) within white matter tracts is a measure of tract integrity and health. Trace (a measure of total, overall diffusion) and mode (Figure 4) are related measures of health and abnormality.

Anisotropic diffusion imaging (DTI), which measures these properties, is a much more sensitive tool than regular MRI for examining the integrity of white matter fiber bundles (Fonov et al., 2007; Figure 3).

PREVIOUS STUDIES
Earlier studies of chronic SZs found significant differences in FA of the UF in the uncinate fasciculus compared to NCs (Kubicki et al., 2002; McIntosh et al., 2008; Sussman et al., 2009), with SZs having lower FA. However, studies of aging in healthy and schizophrenic populations have found decreases in FA overtime, especially in SZs (Mor et al., 2008; Rosenberger et al., 2008); hence aging as well as effects from medication, institutionalization, and duration of illness may all confound the findings in chronic patients.

Recent first-episode and high-risk studies did not find significant UF FA differences compared with controls (Peters et al., 2008; Price et al., 2008).

RESULTS
Statistically significant differences in mean trace between FESZs and NCs in tracts in both the left (p=0.033) and right (p=0.015) hemispheres. (Figure 9)

Trend-level difference in FA on the left side (p=0.085). (Figure 10)

CONCLUSIONS
We found significantly greater trace in the uncinate fasciculi of first-episode schizophrenic patients. These findings indicate greater overall diffusion takes place in FESZ UF tracts. These findings suggest the presence of minor abnormalities in the UF tracts of FESZs. Since the fraction of diffusion that occurs along their white matter fibers is similar to that which occurs in NCs (i.e., FA), it may be that there is more space between fibers in FESZs, which could be caused by abnormal myelination, fewer fibers, or fewer oligodendrocytes between axons.

In the context of previous research, our findings suggest that trace abnormalities are present at first episode and it is possible that these abnormalities worsen over time, although further research is needed to determine whether these findings are progression.

Our age- and overall matching could be improved by recruitment of younger controls and more subjects in general. More subjects may also confirm the trend towards lower FA in FESZs.

Further studies are needed to confirm our findings, and create a clearer picture of white matter connectivity abnormalities in schizophrenia and their progression over time.

REFERENCES