A. THREE MEASURES OF TOBACCO DEPENDENCE INDEPENDENTLY PREDICT CHANGES IN NEURAL STRUCTURE

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E. Studies have demonstrated moderate correlations between fractional anisotropy (FA, a measure of white matter organization), and Fagerström Test for Nicotine Dependence (FTND) scores in various white matter brain structures (r=-.52 to -.64). FA increases with smoking in adolescents, but in adult smokers FA declines with the progression of physical dependence. We examined correlations between FA and 3 measures of tobacco dependence: the FTND, Levels of Physical Dependence (PD), and the Hooked on Nicotine Checklist (HONC). The latter 2 measures assess only symptoms rather than behaviors, based on an assumption that a direct assessment of subjective symptoms will better reflect underlying biological conditions than behaviors that might be constrained by sociocultural factors. We compared white matter FA in 8 smokers and 10 nonsmokers and plotted the location of maximal correlation between FA and each dependence measure. FA trended higher in smokers than nonsmokers in the anterior cingulum bundle (ACb) ($p=0.05$). Among smokers, plots of the maximal correlation for all 3 measures fell within a circumscribed area of the left ACb, showing excellent concordance of results across measures. The maximal correlation with FA was r= -.78 for the FTND, -.85 for Levels of PD, and -.96 for the HONC ($p<0.05$). These data suggest that subjective symptoms reflect the underlying biology better than behavior does. The reliability and validity of the HONC measure is supported by its excellent correlation with FA. The rapid development of HONC symptoms implies that changes in neural density begin with the first cigarettes. This conclusion is supported by other studies showing a significant increase in tissue density in the cingulate cortex; a trend in the same direction in the nucleus accumbens and prefrontal cortex in rats that had received 4 doses of nicotine; and dendritic proliferation among rats in the latter two structures.