approximately 3 days before and 2 days after receiving 25 mg of psilocybin (n = 5) or 50 mg of diphenhydramine (n = 6). Visual alcohol and emotionally valanced (positive, negative, or neutral) stimuli were presented in block design. RESULTS/ANTICIPATED RESULTS: Across both alcohol and emotional cues, psilocybin increased activity in the medial and lateral prefrontal cortex (PFC) and left caudate, and decreased activity in the insular, motor, temporal, parietal, and occipital cortices, and cerebellum. Unique to negative cues, psilocybin increased supramarginal gyrus activity; unique to positive cues, psilocybin increased right hippocampus activity and decreased left hippocampus activity. DISCUSSION/SIGNIFICANCE: Greater PFC and caudate engagement and concomitant insula, motor, and cerebellar disengagement suggests enhanced goal-directed action, improved emotional regulation, and diminished craving. The robust changes in brain activity observed in this pilot study warrant larger neuroimaging studies to elucidate neural mechanisms of PAT.

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Diagnostic Evidence Gauge of Spatial Transcriptomics (DEGAS-ST): Using transfer learning to map clinical data to spatial transcriptomics in prostate cancer†

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OBJECTIVES/GOALS: The 'field effect' is a concept in pathology that pre-malignant tissue changes forecast health. Spatial transcriptomics could detect these changes earlier than histopathology, suggesting new early cancer screening methods. Knowing how normal tissue damage relates to cancer's origin and progression may improve long-term outcomes. METHODS/STUDY POPULATION: We trained DEGAS, our machine learning framework, with prostate cancer data, combining both general cancer patterns and in-depth genetic information from individual tumors. The Tumor Cancer Genome Atlas (TCGA) shows how gene patterns in tumors relate to patient outcomes, emphasizing the differences between tumors from different patients (intertumor). On the other hand, spatial transcriptomics (ST) shows the genetic variety within a single tumor (intratumor) but has limited samples, making it hard to know which genetic differences are important for treatment. DEGAS bridges these areas by finding tissue sections that resemble those in TCGA profiles and are key indicators of patient survival. DEGAS serves as a valuable tool for generating clinically-important hypotheses. RESULTS/ANTICIPATED RESULTS: DEGAS identified benign-appearing glands in a normal prostate as being highly associated with poor progression-free survival. These glands have transcriptional signatures similar to high-grade prostate cancer. We confirmed this finding in a separate prostate cancer ST dataset. By integrating single cell (SC) data we demonstrated that cells annotated as cancerous in the SC data map to regions of benign glands in the ST dataset. We pinpoint several genes, chiefly Microseminoprotein-β (MSMB, PSP94), where reduced expression is highly correlated with poor progression-free survival. Cell type specific differential expression analysis further revealed that loss of MSMB expression associated with poor outcomes occurs specifically in luminal epithelia, the putative progenitor of prostate cancer. DISCUSSION/SIGNIFICANCE: DEGAS reveals that normal-appearing tissue can be highly-associated with tumor progression and underscores the importance of the 'field effect' in cancer research. Traditional analysis may miss such nuance, hiding key transitional cell states. Validating gene markers could boost early cancer detection and understanding of metastasis.

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Social Network Analysis of Patient Sharing Among Providers: Implications for Analyzing Disparities in Cancer Screening

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OBJECTIVES/GOALS: Many providers share patients resulting in networks where clinical information is exchanged, and which can impact the quality and efficiency of care. Here we analyzed the network properties of a primary care service area (PCSA) in Harris County TX, motivating our ongoing analysis of how they are associated with disparities in cancer screening. METHODS/STUDY POPULATION: Data.All providers (n=731, Medicare 2018) from the PCSA with the most providers in Harris County TX, with gender, specialty, and the number of shared patients. Method. Modeled the data as a network consisting of provider nodes, connected in pairs by edges if they shared >11 patients (an empirically-determined threshold). Analyzed the network structure using (1) modularity maximization and its significance to identify densely-connected communities; (2) degree centralization to measure whether a few providers shared many patients, and betweenness centralization to measure whether a few providers connected densely-connected communities; and (3) chi-squared to measure if pairs of connected providers tended to be of the same gender compared to disconnected provider pairs. RESULTS/ANTICIPATED RESULTS: The results (Fig. 1, http://www.skbhavnani.com/DIVA/Images/Fig-1-SNA-Network.jpg [http://www.skbhavnani.com/DIVA/Images/Fig-1-SNA-Network.jpg]) revealed a fragmented network with 120 small components (connected subnetworks, not part of any larger connected subnetwork), and 1 large component. The large component (n=244) had strong and significant modularity (Q=0.73, z=53.13, P<.001) with communities of providers that shared more patients than expected by chance; low degree centralization (dc=0.11) suggesting that no provider dominated patient sharing, in addition to high and significant betweenness centralization (bc=0.5, P<.01) suggesting that a few providers were responsible for connecting the densely-connected communities; and a significant gender bias (X2=10.05, df=1, P< .01) among those that shared patients, versus those that did not. DISCUSSION/SIGNIFICANCE: The analysis revealed a specific type of vulnerability (betweenness) for network fragmentation, and a gender bias in how patients were shared. These results motivated our ongoing analysis on how the network properties are associated with disparity in cancer screening within PCSAs across Texas.

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