scanner. Time-activity curves in regions-of-interest were fitted with multilinear analysis-1 method. Binding potentials (BPND) were calculated using cerebellum as the reference region and corrected for partial volume effects. RESULTS/ANTICIPATED RESULTS: In 5-HT6 rich areas, regional 11C-GSK215083 displayed a negative correlation between BPND and age in the caudate ($r = -0.41$, $p = 0.03$) (14% change per decade), and putamen ($r = -0.30$, $p = 0.04$) (11% change per decade), but not in the ventral striatum and pallidum. Negative correlation with age was also seen in cortical regions ($r = -0.41$, $p = 0.03$) (7% change per decade), consistent with the literature on 5-HT2A availability. DISCUSSION/SIGNIFICANCE OF IMPACT: This is the first in vivo study in humans to examine the effect of age on 5-HT6 receptor availability. The study demonstrated a significant age-related decline in 5-HT6 availability (BPND) in the caudate and putamen.

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Association between source case cavitation on chest radiograph and QuantiFERON-TB Gold In-Tube conversion among close contacts of active tuberculosis cases in Brazil

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OBJECTIVES/SPECIFIC AIMS: QuantiFERON-TB Gold In-Tube (QFT) conversion from negative to positive, is regarded as a marker of recent latent tuberculosis infection and may be predictive of incident active tuberculosis (TB) disease. However, it remains unclear how conversion is influenced by individual and environmental factors, including the infectiousness of the source case to whom the contact was exposed. We aimed to examine the effect of infectiousness of TB in the source case, as measured by presence of cavitation on chest X-ray, on the incidence of QFT conversion among close contacts of the pulmonary TB index case, after adjusting for potential confounding by contact and source case characteristics. METHODS/STUDY POPULATION: The Regional Prospective Observational Research for Tuberculosis (RePORT)-Brazil is an ongoing prospective cohort study that enrolls close contacts of culture-confirmed pulmonary TB patients and follows them for 24 months for development of active TB. Demographic, clinical, and diagnostic information are obtained at baseline and during follow-up at clinical visits and by telephone. QFT testing is performed at baseline and repeated after 6 months if the baseline QFT is negative. A positive IFN-γ value is defined as >0.35 IU/mL, as recommended by the manufacturer and the CDC, and QFT conversion is defined as a negative QFT at baseline followed by a positive QFT at 6 months. RESULTS/ANTICIPATED RESULTS: Among 260 enrolled contacts with nonpositive baseline QFT results and 6 months of follow-up, 198 (76%) were retested with QFT 6 months after enrollment. Of those retested, 26 (13%) converted to positive. Presence of any cavitation in the source case, based on chest radiography, was significantly associated with QFT-conversion (ORunadjusted = 2.4, 95% CI: 1.0–5.7). Additional univariate analyses revealed that QFT conversion was associated with black and brown race (compared with white race) of the contact, current smoking and current alcohol use in the source case. After adjusting for potential confounders (age, sex, and race of the contact and current smoking of the source case), the association between source case cavitation and QFT conversion remained (ORadjusted = 2.5 95% CI: 1.0–6.2). As of December 6, 2017, none of the QFT-retested contacts had developed active TB, with a median follow-up of 12.3 months (IQR: 7.1–13.1). We anticipate that ongoing enrollment and follow-up may yield cases of active TB; future analyses will provide greater precision for examining predictors of QFT-conversion and its association with incident TB. DISCUSSION/SIGNIFICANCE OF IMPACT: Our preliminary results agree with published literature suggesting the infectiousness of TB in the index case is a predictor of incident LTBI. Along with recent LTBI, immune suppression, HIV co-infection, and type 2 diabetes are considered risk factors for progression to active TB disease. Because only a small proportion of persons progress from LTBI to active TB disease, it is not appropriate to treat all persons with LTBI. Thus, more research is needed to identify groups at highest risk for QFT-conversion and incident TB disease, so these groups can be targeted for TB prevention, interventions, and facilitate a decline in TB incidence and mortality.

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Associations between inflammatory markers and negative symptoms in individuals with schizophrenia: Converging evidence

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OBJECTIVES/SPECIFIC AIMS: Negative symptoms of schizophrenia, including motivational deficits, social withdrawal, poverty of speech, decreased emotional reactivity, and psychomotor retardation, have been shown to be most predictive of functional impairment and poor outcome in patients with schizophrenia. Furthermore, these symptoms tend not to be responsive to antipsychotic medications. Inflammation could be one mechanism underlying these difficult to treat symptoms. METHODS/STUDY POPULATION: Three cohorts of patients, reflecting different phases of disease, were studied. One cohort was comprised of a sample of patients with deficit schizophrenia (characterized by primary and enduring negative symptoms; n = 17), nondeficit patients (n = 39), and healthy controls (n = 28). ANOVA and multivariate general linear models were used to compare groups, and linear regression models were used to examine relationships between inflammatory cytokines and negative symptoms. The second cohort was comprised of 80 individuals at clinical high risk for psychosis from the North American Prodromal Longitudinal Study. Linear regression models examined the relationship between baseline inflammatory markers and subsequent negative symptoms at follow-up visits up to 2 years. The third cohort consisted of patients with treatment-resistant schizophrenia (TRS) on clozapine (n = 10). Correlations were performed to examine relationships between inflammatory markers and negative symptoms. In a subgroup of patients from this third sample, resting state functional connectivity analyses were performed on fMRI data to explore relationships between inflammatory markers and connectivity in brain reward circuitry. RESULTS/ANTICIPATED RESULTS: In a sample of patients with the deficit syndrome of schizophrenia (n = 17), a subtype of the disorder characterized by primary and enduring negative Symptoms, tumor necrosis factor (TNF) was significantly increased relative to nondeficit patients (n = 39) and healthy controls (n = 28; $F_{2,57} = 3.51$, $p = 0.036$), and predicted total negative symptoms ($\beta = 0.31$, $p = 0.012$), alogia ($\beta = 0.30$, $p = 0.024$), and blunted affect ($\beta = 0.31$, $p = 0.018$) items of the Positive and Negative Symptom Scale in linear regression models while controlling for antipsychotics. In another sample of individuals at clinical-high risk for psychosis (n = 80), baseline concentrations of TNF significantly predicted negative symptoms, including anhedonia, apathy, and loss of interest in linear regression models, at the 6-month ($\beta = 0.25$, $p = 0.011$) and 12-month follow-up ($\beta = 0.39$, $p = 0.001$). Interleukin (IL)-1 receptor antagonist also predicted these symptoms at the 6-month follow-up ($\beta = 0.21$, $p = 0.037$). In a third sample (n = 10) of patients with TRS treated with clozapine, IL-1β was correlated with passive/apathetic social withdrawal ($r = 0.657$, $p = 0.039$) and disturbance of volition ($r = 0.686$, $p = 0.029$) items of the Positive and Negative Symptom Scale and the global avolition-apathy scores of the Scale for the Assessment of Negative Symptoms ($r = 0.751$, $p = 0.012$). Finally, in a small subsample (n = 5) of patients from this TRS cohort for whom we collected fMRI data, we found resting-state functional connectivity from a right nucleus accumbens seed to a cluster in medial prefrontal cortex. We found relationships between higher inflammation and decreased connectivity for TNF ($r = -0.64$) and CRP ($r = -0.89$). DISCUSSION/SIGNIFICANCE OF IMPACT: Taken together, these preliminary data show the predicted relationship between inflammatory markers and negative symptoms and demonstrate the reproducibility of TNF and other monocytic-derived cytokines as reliably elevated in schizophrenia and associated with negative symptoms across samples of patients with schizophrenia and individuals at high risk for psychosis. Cytokines may exert their effects via their impact on brain reward circuitry, and could represent novel treatment targets for motivational deficits and negative symptoms of schizophrenia.