Request #: 574 - PSY - Dissertation

Oxytocin receptor binding density in schizophrenia

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Background

Schizophrenia is a severe, chronic disorder characterized by a wide range of symptoms, such as hallucinations, delusions, cognitive deficits, and impairments in social cognition. Although antipsychotic drugs are typically effective in treating psychotic symptoms in schizophrenia, the social cognitive symptoms (e.g., social withdrawal, emotion perception deficits) often persist. As social cognitive functioning is predictive of successful life outcomes in schizophrenia, there is a critical need to determine the biological basis of social cognitive impairments in schizophrenia. Due to its ability to affect a wide range of social behaviors in animals and humans, the oxytocin system has become a therapeutic target of interest to treat social cognitive impairments in schizophrenia. Although several studies examine oxytocin in schizophrenia using plasma oxytocin concentrations, plasma oxytocin levels are often not correlated with cerebrospinal fluid oxytocin levels, indicating that plasma oxytocin cannot reliably elucidate oxytocin levels in the brain. Further, the only known study examining oxytocin receptors in schizophrenia is inconclusive, due to overlapping vasopressin receptor binding. Therefore, it is unknown whether there is dysfunctionof oxytocin in the brain in schizophrenia. The current study will use a novel technique to 1) reliably localize oxytocin receptors in schizophrenia 2) quantitatively compare oxytocin receptor binding and oxytocin receptor gene expression in brain tissue from individuals who had schizophrenia relative to matched, unaffected controls 3) determine the effect of age on OXTR density and mRNA expression in the brains of individuals with SZ and in the neurotypical brain . Our findings will be critical to the development of oxytocin therapeutics for treating social impairments in schizophrenia, autism spectrum disorder, social anxiety disorder, and post-traumatic stress disorder.

Sample

Planned sample size: 3 specimens (regions Brodmann's area 21, hypothalamus, substantia nigra) from 21 subjects who had schizophrenia, 3 (regions Brodmann's area 21, hypothalamus, substantia nigra)from 21 unaffected matched controls

Hypothesis

General research questionS: Are there differences in oxytocin receptor binding densities and oxytocin receptor mRNA expression between individuals who had schizophrenia and unaffected controls?

Hypotheses: 1)OXTR binding densities will be reduced in the substantia nigra in SZ relative to unaffected matched controls. 2)OXTR binding in the STS will be correlated with negative symptom severity scores(e.g., social withdrawal)on the Positive and Negative Syndrome Scale 3)locations expressing OXTR mRNA will corroborate OXTR binding sites and densities 4) OXTR binding densities will decrease with age in both the SZ and neurotypical groups. 5) decreases in OXTR binding densities with age will be accelerated in individuals with SZ in the substantia nigra

Progress

I am currently collecting data and have run a power analysis for the linear regression.

Request

Planning analysis. We have a set sample size/number of specimens received from the NIH Neurobiobank, and cannot receive more. Our concern/question is what statistical analysis/linear regression model do we have enough power to conduct? The results from the power analysis indicate that a total sample size of at least 41 is sufficient to detect differences at a large effect size (f^2=.33) with four predictor variables, power set to .80, and an alpha of .05. However, we have 7 potential predictor variables we are interested in including, with some control variables that seem necessary to include in the model if possible, due to known effects on the outcomes (e.g., effects of postmortem interval on mRNA expression).

Timeline

F31 Proposal Resubmission Deadline: December 1st (deadline for the Sponsored Programs office at USU), December 8th (NIH deadline)

The general timetable for the dissertation project: 1) December 8th F31 proposal 2) January 2022 Dissertation proposal (committee) 3) Fall 2022 Completion of data collection, analysis 4) early Spring 2023 Write and submit manuscript 5) end of spring 2023 semester Dissertation defense