

cortex, temporal pole, parietal cortex, and angular gyrus. The identified network was significantly enriched for volumetric alterations in XXY patients relative to controls and a functional association with working memory (via Neurosynth).

**Conclusions:** Individuals with KS demonstrate regionally patterned increases in cerebello-cortical FC relative to XY controls. Overlap between observed regions of increased FC and regions with known structural abnormality provides convergent evidence for loci of cortical alterations that could help explain aspects of the cognitive and behavioral phenotype of KS.

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**Keywords:** Resting State fMRI, Klinefelter's Syndrome, Sex Chromosomes, Neurogenetic Syndromes, Cerebellum

### Peripheral Inflammation Markers Identify a Subset of Patients With Schizophrenia and Related Psychoses who Display Intellectual Decline From Premorbid Levels

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**Background:** Inflammation has been identified in a substantial subset of high-risk and chronically ill patients with schizophrenia and related psychoses which may account for some heterogeneity in schizophrenia. There is also heterogeneity in cognitive deficits related to schizophrenia. However, the relationship between intellectual decline with the illness onset and inflammation in schizophrenia has not been determined.

**Methods:** Here, we report on inflammation markers in independent samples of chronically ill patients with schizophrenia and related psychoses (73 patients versus 70 healthy controls from Sydney, Australia and 297 patients from Syracuse, NY, USA). Peripheral venous blood samples were collected from all participants and markers of inflammation (C-Reactive Protein: CRP, and Neutrophil to Lymphocyte Ratio: NLR) were measured. Premorbid and current intellectual levels were obtained from the Sydney sample.

**Results:** Forty-two percent of the patients versus 20% of the controls had elevated CRP (Chi Square = 9.16,  $p = .002$ ) and elevated mean NLR of 2.5. Peripheral inflammation was confirmed in the Syracuse sample in which 39% had an elevated NLR above the normal cutoff of 2.2. Patients from the Sydney sample who had an elevated CRP also had a significant mean 15-point IQ decline, whereas the patients with normal CRP levels did not show a significant IQ decline.

**Conclusions:** Our study showed evidence of elevated peripheral inflammation markers in subgroups of chronically ill patients with schizophrenia from independent samples and a link between marked intellectual decline and peripheral inflammation suggesting a role for inflammation in the cognitive impairment of a substantial proportion of patients with schizophrenia.

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**Keywords:** Schizophrenia, Schizoaffective Disorder, Schizophrenia Spectrum, General Intellectual Ability, Inflammation, Premorbid Intellectual Ability

### Peripheral Reelin Administration Rescues Corticosterone-Induced Depression-Like Behaviour and Neurochemical Alterations in Male and Female Rats

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**Background:** Depression is characterized by anhedonia and despair and chronic stress is usually a predisposing factor. In our lab, we model depression by administering rats with the stress hormone, corticosterone, for several weeks. Corticosterone-treated rats consistently exhibit cognitive deficits, despair- and anhedonia-like behavior, along with neurochemical alterations associated with depression. These deficits are rescued by antidepressants, as well as intrahippocampally- and peripherally-administered reelin. Reelin regulates neuronal migration, synaptogenesis, and dendritic growth. To date, no studies have addressed sex differences in response to reelin treatment.

**Methods:** In this study, 40 male and 40 female rats were treated with either vehicle or corticosterone for 3 weeks with additional injections of either vehicle or 3µg of peripherally-administered reelin 3 times over the corticosterone-injection period. They were then subjected to the forced swim, sucrose preference and object-location tests, followed by post-mortem analyses of GABAA  $\beta$ 2/3, GluA1, and GluN2B expression. Three-way ANOVAs were used to compare group means.

**Results:** Results show that corticosterone increased depression-like behavior in the forced swim test for both sexes but more so in males, increased anhedonia-like behavior in the sucrose preference test, decreased GABAA  $\beta$ 2/3 and GluA1 expression while increasing GluN2B immunoreactivity (more so in males) in the hippocampus. Reelin rescued depression-like behavior in the forced swim test and the neurochemical alterations, but not sucrose preference. There were no apparent sex differences in response to reelin treatment.

**Conclusions:** Our findings provide further evidence that reelin has antidepressant-like effects. Additional mechanistic and pharmacokinetic studies are a necessity.

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**Keywords:** Reelin, Depression, Corticosterone, Chronic Stress, Rat

### Peritraumatic Anxiety Sensitivity Predicts Post-traumatic Stress Symptoms After Sexual Assault

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**Background:** Anxiety sensitivity (AS), or fear of anxious arousal, has been shown to predict posttraumatic stress symptoms (PTSS) after campus shootings and analogue traumas. Sexual assault (SA) disproportionately impacts women and often results in prolonged PTSS. The prospective association between AS and PTSS has not been evaluated in SA survivors.

**Methods:** Women SA survivors  $\geq 18$  years were enrolled at the time of emergency care. AS (ASI-3, abbreviated) and prior trauma exposure (LEC) were assessed one week after SA. PTSS severity (PCL-5) was evaluated one and six weeks after SA, and generalized linear modeling was used to evaluate the relationship between peritraumatic AS after SA and one- and six-week PTSS severity.

**Results:** A subset of SA survivors ( $n=52$ ) from a larger cohort of SA survivors completed the ASI-3 one week after SA; 48/52 (92.3%) of these women completed six-week follow-up and constitute the study sample. Mean AS score at one week was 2.67 (SD=2.92), PCL-5 scores at one and six weeks were 47.30 (SD=18.19) and 41.17 (SD=19.91). AS predicted PTSS severity with a medium effect size ( $F(1, 46)=5.36$ ,  $p=0.025$ ,  $\eta^2=0.10$ ). Among PTSS clusters, AS predicted increased re-experiencing ( $F(1, 46)=4.86$ ,  $p=0.033$ ,  $\eta^2=0.10$ ) and negative alterations in cognition and mood ( $F(1, 46)=4.59$ ,  $p=0.038$ ,  $\eta^2=0.09$ ). The relationship between AS and total PTSS persisted after adjusting for prior trauma exposure ( $F(1, 46)=4.54$ ,  $p=0.039$ ,  $\eta^2=0.09$ ).

**Conclusions:** Heightened AS is associated with increased PTSS severity after SA. AS may be a useful target within cognitive-behavioral interventions for SA survivors to reduce PTSS and improve recovery.

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**Keywords:** Anxiety Sensitivity, Sexual Assault, Posttraumatic Stress, PTSD, Trauma

### Peritraumatic Circulating 17 $\beta$ -Estradiol as a Resiliency Factor for Chronic Pain Outcomes in Women Following Trauma

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**Background:** Musculoskeletal pain is common following traumatic/stressful life events and is more common in women than men. However, resiliency factors that predict improved chronic posttraumatic musculoskeletal pain (CPMP) in women are poorly understood. In the current study, we examined whether peritraumatic circulating 17 $\beta$ -estradiol (E2) levels influence CPMP trajectories in women.

**Methods:** Peritraumatic E2 levels were measured via ELISA in plasma samples ( $n=167$ ) derived from three multiethnic longitudinal cohort studies of trauma survivors. These cohorts enrolled individuals experiencing motor vehicle collision (MVC,  $n=89$ ), sexual assault ( $n=64$ ), and major thermal burn injury ( $n=14$ ). CPMP (0-10 numeric rating scale) was assessed 6-weeks, 6-months, and 1-year following traumatic stress exposure. Repeated measures mixed models were used to test the relationship between log-transformed E2 levels and CPMP. Secondary analyses of MVC cohort gene expression data ( $n=37$ ) evaluated mediating transcripts and associated biological pathways (Ingenuity, IPA).

**Results:** An inverse relationship between peritraumatic E2 and the development of CPMP was observed ( $\beta = -0.353$ ,  $p=0.033$ ) such that women with high E2 at the time of trauma had less CPMP over the following year. Secondary analyses identified 250 mRNA that mediated the relationship between E2 and CPMP; initial enrichment analyses identified eIF2 signaling as a top pathway through which E2 might influence CPMP development.

**Conclusions:** Increased peritraumatic E2 levels predict improved CPMP outcomes in women.

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**Keywords:** Chronic Pain, Trauma, Estrogen, Women, Sex Differences

### Perturbation-Based Mapping of Subcallosal Cingulate With Deep Brain Stimulation: Cortical Oscillatory Dynamics to Confirm Target for Electrical Neuromodulation

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**Background:** Perturbation-based mapping is an emerging approach to the study of circuit dynamics in the living human brain. Pulses of deep brain stimulation (DBS) to the subcallosal cingulate (SCC) evoke a coherent and reliable cortical response, recorded on the scalp surface with dense array EEG, that may reflect endogenous network dynamics. As precision targeting within the SCC region has been linked to DBS treatment efficacy, we examined features of the cortical perturbation map that change when stimulation is delivered to different locations within the surgical target region.

**Methods:** Cortex-wide effects of stimulation to various locations in the SCC were recorded using dEEG in patients