Associations Between Serotonin Transporter (SERT) Risk Alleles & Parietal EEG Asymmetry

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Abstract

Serotonin is thought to be a powerful neuro-modulator of mood and arousal due to its influence on the pharmacological treatment of psychopathology such as depression & anxiety. Over the past decade, the serotonin transporter (SERT) has been the subject many investigations as a genetic marker for risk for developing psychopathology, with mixed findings. Research also suggests that parietal EEG asymmetry may be used as a marker for risk for developing psychopathology (Stewart et al, in press), with individuals who demonstrate greater relative left parietal activity hypothesized to be at greater risk. The current study investigated the relationship between serotonin transporter (SERT) genotypes and parietal asymmetry (insertion/deletion ("long" and "short") to patterns of regional electrical brain activity. The sample consisted of 366 volunteers (113 males) aged (18-34). EEG was averaged from 64 scalp sites on four days (two 8-minute periods each day), and transformed to current-source density prior to extraction of alpha band activity via FFT. There was a main effect of 3SERT genotype such that individuals who carried at least one copy of the short (risk) allele showed greater relative left parietal activity (less left parietal alpha) at channel pairs P7/P8, P3/P4 & P1/P2. These results indicate the importance of genetic contributions to psychopathology and possible risk for psychopathology.

Introduction

Depression is a heterogeneous illness with individual phenotypes indicating little about illness etiology, but indicating multiple disease pathways and the interactions of genes and environment.

Methods

Participants: 106 volunteers (31% male) aged 18-34 (M=19.2; SD=2.0). 163 participants had a history of Major Depression (MDD+); the other 143 had no history of depressive illness (MDD-).

Gene/Alleles: The Serotonin Transporter Gene (SERT: SLCE6A4: 44bp insertion/deletion results in two distinct alleles, a “long” version, including the 44bp insertion and the “short” version, excluding it. The short allele is considered the risk allele.

Electrophysiology Data Collection & Processing:

Resting EEG data were collected on four separate days within a 14-day window, two 8-minute periods each day.

EEG was recorded continuously using 64-channel EEG cap with 1K Hz sampling rate (bandpass 0.200 Hz) using online reference just posterior to Cz, re-referenced offline using current source density (CSD) algorithm (Keysar & Tenke, 2006).

Followling offline ocular rejection of vertical EOG amplitude greater than ±275°, data were segmented to 2.684 s epochs, windowed with a Hamming taper, and power in alpha frequency band (8-13Hz) was extracted via Fast Fourier transformed (FFT).

Parietal Asymmetry:

Alpha asymmetry scores, In-transformed subtractions (In[Right]-In[Left]) between homologous sites were calculated, providing an asymmetry score for each session and day. The following parietal channel pairs were statistically examined: P1/2, P3/4, P5/6 & P7/8. Greater values signify relatively greater right alpha power, relatively less right activity. Statistical Analysis:

Mixed Linear Models: DV: Asymmetry score at each channel pair IVs: Day, Session, MDD Hx (+/-), SERT risk (+/-) Covariate: Z-scored total number of recent life events

Results

Summary: There was a main effect of Genotype significant at all channel pairs. Pairwise comparisons indicated risk genotype predicted relatively greater left parietal activity (Figure 3).

Discussion

These findings support a relationship between serotonin transporter gene variants and parietal EEG asymmetry. Individuals who carried at least one copy of the short allele show relatively greater left parietal activity (Figure 1).

There were significant genotype by stressful life events interactions at each site with risk allele carriers who had experienced a greater number of life events showing relatively greater left parietal activity.

The relationship between SERT genotype and stressful life events was further moderated by MDD Hx (+/-) such that individuals with a risk genotype, a history of MDD (cured of past), and a greater number of stressful life events, consistently display greater left parietal activity, compared to their never depressed counterparts.

Regardless of MDD Hx, individuals with risk genotypes may not necessarily experience mood disturbance simply as a function of genotype. However, those same individuals could be at a disadvantage when faced with life stress. Less efficient serotonergic systems would be more likely to break down under greater allostatic load.

Follow up research is warranted to ascertain the extent of this risk conveyance, particularly, tracking over time individuals considered at risk for depression based on genotype and resting brain activity.

These data partially support the potential utility of parietal EEG asymmetry and SERT genetic variants as an endophenotypes of risk for psychiatric disorder, and suggest the promise of identifying individuals at risk who carry either (or both) of these endophenotypes and how life stress may tax a vulnerable diathesis placing an individual at risk for psychophatogy or possible relapse.

References


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