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Frontal asymmetry index in Williams syndrome: Evidence for altered emotional brain circuitry?

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Abstract

Asymmetrical frontal EEG activity is associated with motivational neural systems of approach/withdrawal behaviors. Greater left frontal EEG has been linked to increased appetitive tendencies whereas increased right frontal activity is related to the activation of avoidance mechanisms. Williams syndrome (WS) is a genetic condition characterized by a highly sociable personality manifested by a propensity to approach strangers and decreased social fear. Consequently, the current study was designed to investigate frontal cortical activity during resting state, indexed by relative alpha power, in adults with WS as compared to typically developing (TD) controls, and a subgroup of TD extraverts. Results indicated that participants with WS produced attenuated left frontal activity relative to TD peers, or TD extraverts in particular; yet, no groups differed in their degree of right frontal activity. Finally, while both TD group and the extravert subset showed trends of greater left over right frontal activity, the WS participants demonstrated opposing effect of increased right over left frontal EEG. Importantly, individuals with WS produced deviating frontal activity patterns compared to TD extraverts despite exhibiting common social-affiliative tendencies, underscoring that neural mechanisms that give rise to extraversion in WS may not function similarly to those subserving this personality trait expressed in TD.

Keywords

Williams syndrome; social neuroscience; extraversion; alpha power; resting EEG

Introduction

Williams syndrome (WS) is a condition marked by a genetic microdeletion on chromosome 7q11.23 (Ewart, Jin, Atkinson, Morris, & Keating, 1994). The WS phenotype typically

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consists of an overfriendly demeanor, increased empathetic gestures, heightened attention to social stimuli (i.e., faces), and an unusual proclivity towards approaching strangers (Järvinen, Korenberg, & Bellugi, 2013). Individuals with this condition display social paradoxes, which include endorsing personality traits representing the desire to develop affectionate and close relations with others (Klein-Tasman & Mervis, 2003) coupled with an unusual inclination to trust others (Riby, Kirk, Hanley, & Riby, 2014), yet juxtaposed with an impaired capacity to foster and sustain peer relations (Gosch & Pankau, 1994) and pronounced anxiety (Dykens, 2003). Notably, the known genetic profile of WS offers a rare avenue to link gene-phenotype associations and elucidate related neural mechanisms that underlie sociability. As such, by applying WS as a model to understand human social behavior, neuroscientists can better clarify the disrupted neurobiological systems contributing to social disorders such as autism spectrum disorder.

Despite the well-established social behavioral profile of WS (Järvinen et al., 2013), the neural substrates of the hypersociability in WS are not well understood. However, the past decade of neuroscience research has proffered that dysregulated activity and circuitry in the frontal and amygdala regions are associated with the atypical affiliative characteristics in WS. Indeed, functional neuroimaging studies (Meyer-Lindenberg et al., 2005) have indicated that deficits in the awareness of social dangers in WS individuals may reflect their reduced amygdala reactivity specific to social threats (e.g., fearful faces) relative to threatening scenes, suggesting the anxiety in WS is uniquely non-social in nature. In a similar vein, our group provided evidence that the diminished amygdala activation towards fearful facial expressions in adults with WS is associated with their self-reported social approach behaviors towards strangers (Haas et al., 2010). Further fMRI findings associated the exaggerated sociability exhibited by these individuals with the anomalous recruitment of the frontal-striatal circuits related to behavioral inhibition, specifically with disrupted connections between striatum and inferior frontal gyrus (Mobbs et al., 2007), and reduced activation of prefrontal regions (i.e., dorsolateral prefrontal cortex, dorsal anterior cingulate cortex). Taken together with documented reports of social disinhibition in those with WS (Little et al., 2013; Riby et al., 2014), results from Mobbs and colleagues (2007) underscore the hypothesis by Porter and colleagues (2007) that altered frontal circuitry may impair response inhibition. Most recent findings further supported that the WS social profile is linked to atypical frontal activity, as demonstrated by increased recruitment of medial rather than lateral orbitofrontal cortex (OFC) in response to negative affective faces in adults with WS, contrary to the pattern of exclusive OFC activation towards positive emotional faces shown by typically developing (TD) individuals (Mimura et al., 2010). Considering that the lateral OFC is typically associated with processing of stimuli with punitive value whereby medial OFC is linked to processing rewarding stimuli (Kringelbach & Rolls, 2004), the findings by Mimura et al. suggest that the ‘hypersocial’ behavioral patterns in WS may stem from abnormalities in the affective reward/punishment circuitry in the frontal cortical region. Altogether, frontal and limbic regions are prominently implicated in the social profile of WS, likely by related disruptions in their social-affective evaluative and inhibitory faculties.

Notably, within normative literature, uneven, or asymmetrical frontal cortical activation has been linked to processing of emotional information and differentially associated with

appetitive/avoidance behaviors (for reviews of resting frontal activation, see Coan & Allen, 2004; Davidson, 1993; Fox, 1991, 1994). Approach/withdrawal model based on frontal resting electroencephalography (EEG) and linked to emotion processing has been postulated (Davidson, 1993, 1998; Fox, 1991, 1994), and applied by social neuroscientists to explain the individual differences in affect and personality traits such as sociability and shyness in TD individuals (Schmidt, 1999). Substantial literature documenting asymmetrical processing and regulation of emotions, and behavioral activation/inhibition supports the proposed model. For instance, Davidson and coauthors (1990, 1993, 1998) reported that adults with increased right over left frontal activation in response to emotional films appraise films with negative emotional content more negatively than their peers who showed opposing EEG patterns of augmented left over right frontal EEG; at the same time, the latter group rated films with positive affective content as more positively emotional. Additionally, these frontal asymmetry patterns appear to be related to emotion regulatory strategies, with greater relative right frontal EEG associated with the ensuing startle potentiation in response to negative emotional stimuli, and greater relative left frontal EEG linked to the suppression of negative affect (Jackson, Burghy, Hanna, Larson, & Davidson, 2000). These findings and those by others (Harmon-Jones & Sigelman, 2001; Harmon-Jones et al., 2004; Santesso, Dana, Schmidt, & Segalowitz, 2006; Schmidt & Trainor, 2001) have contributed to establishing the link between frontal asymmetry (i.e., greater relative left/right frontal EEG activity) and affective processes related to appetitive/avoidance motivation.

This relationship is often considered in the context of Gray's proposed behavioral activation/inhibition systems (i.e., BAS, BIS), according to which those with high degree of BAS are more sensitive to rewards, respond to reinforcement cues in positive manner, and are oriented towards achieving their goals; whereas, high BIS individuals are more sensitive to punishment and display more avoidance tendencies in efforts to prevent aversive consequences (Gray, 1972, 1981, 1987, 1990). Moreover, those with high BAS generally experience more positive emotionality compared to those high on BIS, who alternatively are subjected to more states of anxiety (Carver & White, 1994). Studies utilizing resting state EEG have provided significant support for this model, demonstrating that increased left over right frontal EEG is associated with greater endorsement of BAS (Coan & Allen, 2003; Harmon-Jones & Allen, 1997); however, evidence regarding the hypothesized relationship between increased BIS and greater right frontal activation (Davidson, 1998; Sutton & Davidson, 1997) is inconsistent (Coan & Allen, 2003; Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997). Nonetheless, investigations focusing on personality traits further underscored that individuals characterized by greater social approach behaviors (i.e., highly sociable, low in shyness) produce relatively greater left frontal activity, whereas those low on sociability and high on shyness demonstrate more activity in the right corresponding hemisphere (Schmidt, 1999). Overall, an abundance of evidence broadly illustrates a relationship between sociability and emotionality, on the one hand, and frontal asymmetry on the other.

In light of this evidence, and given the behavioral tendencies such as high sociability and overt positive emotionality observed in individuals with WS, the present study aimed to investigate whether those with WS would demonstrate frontal asymmetry patterns consistent with their sociability and extraverted approach. To this end, we examined the left/right

frontal EEG activity in adults with WS relative to TD counterparts, as well as relative to a subset of TD controls characterized as extraverts. Based on the social phenotype of WS, we hypothesized that individuals with WS would exhibit an increased left over right frontal asymmetry pattern, mirroring their unusual hypersociability and propensity to approach strangers (Järvinen et al., 2013).

Methods

Participants

Nine adults with WS (4F; $M=31.33$ years, $SD=8.23$) and 16 healthy TD individuals (6F; $M=20.13$ years, $SD=1.78$) participated in the current study for a pecuniary compensation. Participants with WS completed a fluorescent in situ hybridization test to determine the presence of the elastin gene deletion, diagnostic of the condition (Korenberg et al., 2000). Inclusion in the TD group required the absence of: significant medical history of neurological or central nervous system (CNS) disorder or trauma, current of past psychiatric disorder, and current medication or substance use that may interfere with CNS functioning. The WS participants were recruited as part of a longstanding multisite program project; as such, the WAIS-III (Wechsler, 1997) was used in continuation of the ongoing program project to evaluate their intellectual functioning. TD participants, however, recruited particularly for this study, were administered the WASI (Wechsler, 1999) as a brief measure of cognitive ability. In line with previous studies (Searcy et al., 2004), those with WS scored lower on VIQ, PIQ and FIQ ($M_{VIQ}=70.00$, $SD_{VIQ}=7.27$; $M_{PIQ}=63.44$, $SD_{PIQ}=6.79$; $M_{FIQ}=64.67$, $SD_{FIQ}=6.80$) than the TD counterparts ($M_{VIQ}=114.50$, $SD_{VIQ}=9.19$; $M_{PIQ}=113.38$, $SD_{PIQ}=8.16$; $M_{FIQ}=115.81$, $SD_{FIQ}=7.31$).

Following the resting state EEG data collection, TD participants completed the Extraversion scale from the NEO Personality Inventory Revised (NEO PI-R; Costa & McCrae, 1992), in order to obtain individual Extraversion T-scores based on the gender-specific normative information outlined in the inventory manual. According to NEO PI-R conversion procedures, T-scores > 65 are considered very high degree of extraversion, while scores 56 to 64 are designated as high. T-scores of 45 to 55 are considered average, while scores 35 to 44 are considered low and scores < 35 as very low. Those TD participants scoring in high and very high range (T-scores > 55) were designated as extraverts for the purpose of this study. As a result, of the 16 TD participants ($M_{NEO}=55.25$, $SD=11.09$), nine were included in the Extraverts subsample ($M_{NEO}=63.44$, $SD=5.00$; 6F; $M_{Age}=20.00$, $SD=1.32$).

EEG Data Acquisition and Processing

Resting state EEG was collected while participants sat in a room customized to minimize noise interference. The EEG was acquired over six 30-second blocks (eyes opened—eyes closed—eyes open—eyes closed—eyes open—eyes closed) using NetStation 4.0 and a 64-channel Geodesic Sensor net with Ag/AgCl electrodes (Electrical Geodesics Inc.). EEG data were filtered through 0.1-40Hz bandpass, referenced to an average mastoid reference, segmented into 1.5 seconds segments, separately for eyes-opened and eyes-closed blocks (with 60 1.5-second-long segments in each condition), and subjected to an Independent Component Analysis (ICA; Jung, Makeig, Westerfield, Townsend, Courchesne, &

Sejnowski, 2000) for detection and correction of eye blinks and lateral eye movement artifacts. The ICA-based artifact rejection procedure allowed retention of most of the trials for analysis. After excluding trials associated with large biological or technical artifacts, we resulted with a mean of 54 / 60 trials per condition (89% for the WS group; 90% for the TD group; $p = 0.79$).

The approximation of spectral power in alpha frequency bandwidth (8-13 Hz) was obtained through Fourier transform with hamming window of 10% in line with Hofman and Schutter (2012). In accordance with previous research implicating frontal-central EEG asymmetry in approach/withdrawal motivational mechanisms (for a recent review see Coan & Allen, 2004), our regions of interest consisted of the following electrodes on the Geodesic Net: Right-channels 2, 3, 54, 55, 57, 58, 62 (corresponding 10-10 channels: AF4, F2, F4, F6, FC2, FC4, FC6); Left-channels 5, 8, 9, 12, 13, 16, 17 (corresponding to 10-10 channels: AF3, F1, F3, F5, FC1, FC3, FC5). Averages of the EEG from the seven electrodes were obtained as indices of mean spectral power of the corresponding frontal hemispheric cortex. Subsequently, these power values were log transformed by applying natural log computations. Notably, alpha power is inversely related to brain activity, such that larger alpha power represents lower brain activity and vice versa. Mean spectral power asymmetry was finally calculated applying the following equation: $\ln(\text{Power}_R) - \ln(\text{Power}_L)$.

Statistical Analysis

Spearman bivariate correlations were computed across participant groups to evaluate the relationship between age, IQ scores and natural log-transformed alpha power values for the right and left hemispheres as well as EEG asymmetry. A 2 (Group: WS, TD) $\times$ 2 (Hemisphere: Right, Left) repeated measures ANOVA was first applied to natural log-transformed alpha power values to examine group differences in hemispheric frontal asymmetry. An independent-samples t -test was computed to evaluate group differences in the degree of alpha power in left versus right frontal regions. In a secondary analysis, the ANOVA and t -test were repeated to evaluate the differences between alpha power asymmetry and hemispheric activity in WS versus TD Extraverts.

Results

Correlations between IQ (VIQ, PIQ, and FIQ) and alpha power of left/right frontal regions and alpha power asymmetry did not reach significance in TD participants, and within the subgroup of Extraverts, $rs < .33$, ns . Within the WS group, the association between VIQ and alpha power asymmetry emerged as marginally significant, $r(9) = .60$, $p = .09$. Figure 1 illustrates the resulting associations between age and left/right frontal alpha power and alpha power asymmetry in WS and TD Extraverts. A negative correlation between age and alpha power of right frontal region was observed in the TD group, $r(16) = -.50$, $p = .05$; whereas this relationship was observed in both left ($r(9) = -.79$) and right hemispheres ($r(9) = -.76$) within the extraverts subsample (both $ps < .02$). Within those with WS, a significant negative association between age and frontal asymmetry emerged, $r(9) = -.87$, $p = .002$, accompanied by marginally significant positive correlations between age and right, $r(9) = .59$, $p = .10$, and left frontal alpha power, $r(9) = .65$, $p = .06$. Altogether, while in the whole

TD cohort there were weak associations between age and their right/left frontal activity or alpha power asymmetry, TD Extraverts, on the other hand, exhibited greater frontal activity (decreased alpha power) across both hemispheres with age, in contrast with the opposite pattern of decreased frontal activity (greater alpha power) with age observed in the WS group. While no relationship between age and frontal asymmetry was observed in both TD and the subgroup of Extraverts, participants with WS showed decreased alpha power asymmetry, reflecting greater relative right frontal activity.

Left versus Right Frontal Alpha Power

Figure 2 illustrates the observed alpha power in right and left frontal regions in TD participants, subgroup of TD Extraverts, and adults with WS. Repeated measures ANOVA yielded both marginally significant effect of Group, $F(1,23)=3.98$, $p=.06$, $\eta^2=.15$, and interaction of Group $\times$ Hemisphere, $F(1,23)=3.81$, $p=.06$, $\eta^2=.14$. Importantly, increased alpha power corresponds to reduced frontal activity, such that the two constructs are inversely associated. Relative to TD group ($M=2.39$), the WS participants produced mildly reduced frontal activity as reflected by higher alpha power ($M=2.65$). To further examine the resulting interaction, independent-samples t -tests were applied to assess the discrepancies between TD and WS participants in left and right frontal activity. TD controls exhibited greater mean spectral alpha power in the left frontal region ($M=2.40$) compared to those with WS ($M=2.62$; $t(23)=2.16$, $p=.04$); whereas, only a minor increase in the right frontal region was observed in the TD group ($M=2.40$) relative to the adults with WS ($M=2.62$; $t(23)=1.76$, $p=.09$). Within each participant group, paired t -tests revealed no differences in resting state frontal activity of left versus right hemisphere, $ts < 1.78$, $ps > .11$.

Analogous computations were implemented to compare resting state EEG between individuals with WS and a subset of TD Extraverts. The main effect of Group (WS vs. Extraverts) was marginally significant, $F(1,16)=3.50$, $p=.08$, $\eta^2=.18$, with greater frontal cortical activity in resting state in Extraverts ($M=2.35$) than in adults with WS ($M=2.65$). A significant interaction of Group $\times$ Hemisphere was found, $F(1,16)=5.37$, $p=.03$, $\eta^2=.25$. Similar to the comparison with the entire TD sample, WS group showed mildly decreased left frontal activity ($M=2.68$) than the Extraverts ($M=2.33$; $t(16)=2.07$, $p=.06$); however, this difference was not observed between Extraverts ($M=2.40$) and individuals with WS ($M=2.62$) in the right frontal cortex, $t(16)=1.62$, $p=.13$. No within-group differences were found, $ts < 1.78$, $ps > .11$. Taken together, TD controls generally demonstrated greater frontal activity, predominantly localized in the left hemisphere, than those with WS.

Alpha Power Asymmetry

Independent t -test showed a marginally greater asymmetry in the WS group in comparison to TD controls, $t(23)=1.95$, $p=.06$. Adults with WS had an average asymmetry of $-.06$, indicative of less left and more right frontal activity at rest. Conversely, TD participants yielded an average alpha power asymmetry of $.02$, which reflects the opposite pattern of cortical activation (i.e., more left and less right frontal activity). Notably, while 8 of 9 participants with WS showed a trend of greater right over left frontal activity, only half of the 16 TD controls showed this trend. Overall, those with WS were more likely to produce elevated right frontal EEG at rest than TD counterparts, $\chi^2(1, N=25)=4.89$, $p=.03$.

As shown in Figure 3, a parallel yet more robust group discrepancy between WS and Extraverts was found, $t(16)=2.32, p=.03$. Extraverts had an average asymmetrical alpha power of .04; thereby, these individuals high on extraversion demonstrated even greater elevated left as compared to right frontal activity than the larger TD group. Of the 9 extraverts, only 3 participants showed the trend of elevated right over left frontal EEG, providing greater support for the unique relationship between right-dominated frontal asymmetry and WS, $\chi^2(1, N=18)=5.84, p=.02$. Altogether, despite the insignificant within-participant differences in left versus right frontal activity, a pattern of divergent asymmetry indices was observed in WS versus TD peers with regard to the frontal EEG activity. Moreover, comparisons between individuals with WS and TD Extraverts produced yet even stronger contrast in frontal activation, indicating that frontal cortical functioning in WS is unlike that of typical Extraverts, despite similarities in overt social behaviors.

Discussion

The central aim of the present study was to investigate whether frontal activity at resting state in individuals with WS resembles that of TD Extraverts. Our predictions were motivated by the extant literature on frontal resting EEG in congruence with Gray's behavior activation/inhibition systems model and emotion processing (see Coan & Allen, 2003, 2004; Fox 1991, 1994). To date, evidence illustrates an association between alpha asymmetry pattern of elevated right over left frontal activity during resting state with increased appraisal of, and subsequent response to negative emotional content, reduced sociability, and greater behavioral inhibition; on the contrary, greater left over right frontal EEG is associated with intensified experience of positive affect coupled with greater suppression of negative emotional reactivity, reduced shyness, and increased appetitive or approach manifestations (see Coan & Allen, 2003, 2004; Davidson, 1998; Schmidt, 1999; Schmidt & Trainor, 2001). As such, those with WS were expected to demonstrate the frontal EEG patterns similar to those observed in TD individuals who express high appetitive drive and gregarious traits, i.e., extraverts.

Our main finding, however, was that individuals with WS produced an opposite frontal EEG pattern from that found in the TD Extraverts, i.e., greater right over left frontal alpha power asymmetry in the former in the face of greater left over right asymmetry in the latter. Group comparisons of frontal EEG across hemispheres further indicate that the contrasts in asymmetry patterns between individuals with WS versus TD were primarily driven by differences within the left frontal EEG. TD adults, whether extraverts or not, showed greater left frontal alpha power than those with WS; whereas, no group differences emerged in right frontal EEG, implicating that the diverging asymmetry patterns between groups were driven by attenuated neural recruitment of the left hemisphere at resting state in WS. Consequently, current results implicate that adults with WS have an altered social-emotional brain circuitry relative to TD individuals, including TD Extraverts.

On the other hand, the emerging frontal asymmetry pattern in WS resembles their psychopathological profile, i.e., augmented stress reactive traits and intensified anxieties (Dykens, 2003; Klein-Tasman & Mervis, 2003; Ng, Järvinen, & Bellugi, 2014). Greater right frontal activity during rest is associated with anxiety (Nitschke, Heller, Palmieri, &

Miller, 1999; Wiedemann et al., 1999). Further, some data suggest that the joint experience of negative affectivity and anxiety is associated with relatively greater right frontal EEG (cf., Thibodeau, Jorgensen, & Kim, 2006). Relative increased right frontal EEG has also been associated with increased startle response, a physiological fear reaction, towards negative affective stimuli (Jackson et al., 2000). In aggregate, increased relative right frontal activity at rest has associations with greater internalizing behavioral disturbances. Indeed, a diathesis-stress framework that has been increasingly applied within the neuroscience field suggests that frontal asymmetry index may function as a stable attribute that increases one's susceptibility to internalizing or mood disorders (cf., Coan & Allen, 2004). As such, it is possible that within those with WS, frontal asymmetry favoring right frontal activity serves as a trait marker predisposing these individuals towards experiences of general anxiety and negative affectivity.

A second original result is the contrasting pattern of relationship between age and frontal asymmetry in adults with WS vs TD participants. Within the WS group, older individuals exhibited greater right over left frontal EEG; whereas, no pattern between age and frontal asymmetry index emerged in TD individuals. Considering sociability associated with WS is relatively stable across age groups (Doyle, Bellugi, Korenberg, & Graham, 2004), this pattern of neural activity at resting state might reflect modifications in the clinical features that are often masked by their 'hypersocial' demeanor. Indeed, researchers have reported that prevalence rates of anxiety disorders are more elevated in older individuals with WS, i.e., young adults and adolescents, than children with the condition (Leyfer et al., 2006; Switaj, 2000), while our recent investigation found no age-related change in sociability traits such as gregariousness and people-oriented attributes (Ng et al., 2014) or approachability ratings (Fishman, Yam, Bellugi, & Mills, 2011).

Notably, this association between age and frontal asymmetry was not found in the TD group, in line with previous findings by developmental investigations, which indicated frontal asymmetry is relatively stable. Frontal alpha band and asymmetry in TD adults are notably more stable and consistent than other frequency bands during test-retest experiments ranging from 3-week to 3-year intervals (Tomarken, Davidson, Wheeler, & Kinney, 1992; Hagemann, Naumann, Thayer, & Bartussek, 2002; Vuga et al., 2006). However, these assertions have been challenged by research highlighting the positive effects of intervention or medication on neural circuitry, i.e., attenuation in relative right frontal activity and mood disturbances in individuals with affective psychopathology (e.g., depression, anxiety) (cf., Coan & Allen, 2004). To date, it remains unclear whether frontal asymmetry represents a stable individual index, reorganizes in response to novel experiences, or differs in mutability as a function of one's clinical status (i.e., normative development, psychiatrically classified, genetically atypical). Given the lack of longitudinal research exploring these variables, our postulation that the observed links between age and rightward frontal EEG asymmetry in WS mirror their clinical presentation is a theoretical conjecture. More systematic research is essential to elucidate the functional basis for alterations/stability in the frontal circuitry throughout development, and to what extent this neural reorganization augments or attenuates risk for the sequelae of psychopathology.

Overall, results of the present study contribute to the growing body of neuroscientific research on WS by demonstrating disturbances in social-emotional neural circuitry in people with WS relative to TD extraverts. Evidenced by their frontal asymmetry at resting state, individuals with WS who are characterized by exaggerated sociability and friendliness exhibited neural processes, known to be associated with affective motivations, opposite to those seen in TD Extraverts. Importantly, the resulting pattern of heightened right over left frontal EEG observed in WS may reflect underlying neural attributes related to their reported fears and anxieties (Dykens, 2003; Leyfer et al., 2006; Switaj, 2000).

In the face of these novel findings, more research is necessary to further understand the relationship between the neurophysiological profile of those with WS and their social phenotype. The present study's focus on frontal asymmetry, motivated by the large literature implicating the frontal EEG and approach/avoidance behaviors, can be extended with further investigations of resting EEG in other sites, to better delineate the neurophysiological function underlying the social behavioral profile associated with WS. In particular, a whole-brain analysis may illustrate the specificity of the right over left EEG asymmetry for the frontal lobes. Secondly, future research would also benefit from a measure of real-life social behaviors (e.g., observations of interpersonal gestures) to better understand the association between the gregarious personality of individuals with WS and their resting EEG profile. For example, future studies can assess whether the frontal asymmetry indices are associated with high empathic concern for others, or social disinhibition characterizing individuals with WS (Järvinen et al., 2013). Finally, among limitations of our study is a small sample size. As such, the mean age difference between the WS and TD groups constrained our interpretation of the associations between age and frontal asymmetry in those with WS and TD. The small sample size did not allow for an exploration of gender effect on the observed association between frontal EEG and sociability. Notably, emerging research indicates that resting EEG can vary as a function of phase within the menstrual cycle (cf., Cacioppo et al., 2013). However, we were unable to further control for hormonal state in this relatively small sample.

Importantly, to adequately address the empirical questions pertaining to the development of frontal alpha asymmetry during rest, future investigations in WS will need to apply developmental approaches such as the application of longitudinal design, and greater integration of interdisciplinary methods (e.g., EEG, autonomic measures, behavioral and cognitive indices). It is through the employment of a multilevel approach that investigators could offer a more cogent and detailed illustration of the social phenotype associated with the elastin gene deletion defining this syndrome. All in all, to our knowledge, the current study is the first to directly compare the emotion neural circuitry of individuals with WS with that of TD, and TD Extraverts in particular. Our main finding shows that individuals with WS possess a social-emotional neural circuitry that is anomalous relative to TD individuals, and specifically, TD Extraverts; thereby, sociability presented in WS is not sustained by the neural operations that support typical extraversion.

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Figure 1. Correlation between age, left and right frontal alpha power during resting state, and alpha power asymmetry in Typically Developing participants (N=16) versus adults with Williams Syndrome (N=9).

Figure 2.

Alpha power of left and right frontal region during resting state in typically developing participants (N = 16), a subset of typically developing extraverts (N = 9), and adults with Williams syndrome (N = 9). Increased ln transformed alpha power values denote less cortical activity.

Figure 3. Alpha power asymmetry during resting state in participants with Williams syndrome ($N = 9$) versus typically developing extraverts ($N = 9$). Greater asymmetry values denote more left frontal activity at resting state.