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Frontal slow wave resting EEG power is higher in individuals at Ultra High Risk for psychosis than in healthy controls but is not associated with negative symptoms or functioning

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ABSTRACT

Decreased brain activity in the frontal region, as indicated by increased slow wave EEG power measured by electrodes place on the skull over this area, in association with negative symptoms has previously been shown to distinguish ultra-high risk (UHR) individuals who later transitioned to psychosis (UHR-P) from those who did not transition (UHR-NP). The aims of the current study were to: 1) replicate these results and 2) investigate whether similar association between increased frontal slow wave activity and functioning shows any value in the prediction of transition to psychosis in UHR individuals. The brain activity, recorded using EEG, of 44 UHR individuals and 38 healthy controls was included in the analyses. Symptom severity was assessed in UHR participants and functioning was measured in both groups. The power in the theta frequency band in the frontal region of UHR individuals was higher than in controls. However, there was no difference between the UHR-P and the UHR-NP groups, and no change in slow frequency power following transition to psychosis. The correlation between delta frequency power and negative symptoms previously observed was not present in our UHR cohort, and there was no association between frontal delta or theta and functioning in either group. Increased delta power was rather correlated with depressive symptoms in the UHR group. Future research will be needed to better understand when, in the course of the illness, does the slow wave activity in the frontal area becomes impaired.

1. Introduction

Psychosis can result in lifelong functional impairments and comorbidities. Schizophrenia, one of the most common psychotic disorders, is strongly associated with poor executive functioning (Martin et al., 2015) and functional impairments (Green, 1996). Early intervention in psychosis is crucial, as deterioration can occur very aggressively in the early phases of the illness (Birchwood et al., 1998; McGorry et al., 2008). Decreased duration of untreated psychosis is associated with better outcomes, i.e., symptomatic and functional remission and better quality of life (Jaracz et al., 2015). Therefore it is important to identify individuals as early as possible in the course of the illness in order to minimize the duration of untreated attenuated psychotic symptoms, maximize therapeutic engagement and treatment, and potentially prevent or delay the onset of psychosis. The importance of identifying individuals in the pre-psychotic phase led to the development of a set of criteria to identify those individuals deemed at increased risk for psychosis or ultra-high risk (UHR) for psychosis.

Transition rates can be as high as 36% after three years (Fusar-Poli et al., 2013) and individuals can transition up to ten years after having been identified as UHR (Nelson et al., 2013). Although these rates seem to be decreasing (Nelson et al., 2013; Yung et al., 2007), early identification and intervention remains a principal goal in clinical practice. It is essential to improve the identification of UHR individuals to further enhance the close-in strategy aimed at detecting true positives in the UHR cohorts. The identification of *endo*-phenotypes or physiological biomarkers that are specific to UHR individuals could improve the predictive power needed in the field of early intervention.

The reduction in executive functioning in the frontal region is a well-documented phenomenon in schizophrenia (see reviews: Boutros et al., 2008b; Galderisi et al., 2009), first-episode psychosis (Harris et al., 2006) and UHR (Lavoie et al., 2012) and could be caused by structural brain abnormalities and/or hypometabolism in the frontal lobe.

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Particularly in individuals with chronic schizophrenia there is reduction of cortical thickness in the bilateral ventromedial prefrontal cortices (Zhang et al., 2015) and hypometabolism in the right dorsolateral prefrontal cortex (Wolkin et al., 1992). Significant decrease in grey matter, white matter and cerebrospinal fluid in the frontal region has all been observed in first-episode schizophrenia as compared to healthy controls (Asami et al., 2012). Similar anatomical changes in the brain can also be seen before the onset of psychosis. Indeed, reduction of grey matter in the frontal region has been found prior to onset of frank psychotic symptoms in individuals with prodromal psychotic symptoms (Pantelis et al., 2003). Frontal hypometabolism in schizophrenia has been associated with negative symptoms (Wolkin et al., 1992), cognitive deficits (Karbasforoushan et al., 2015) and functional deficits (Tully et al., 2014).

However, these frontal deficits are not unique to psychosis and are present in other psychiatric illnesses such as in anxiety (Park et al., 2016) and depression (Tomioka et al., 2015). Therefore, it is worthwhile investigating these frontal deficits in more detail, particularly in terms of their possible relationship with increased risk of transition to psychosis in the UHR population.

Most studies have used positron emission tomography or functional magnetic resonance imaging to investigate deficits in frontal activity. However, electroencephalography (EEG) may present a more convenient way to evaluate frontal deficits. Indeed, measurement of resting brain activity using EEG has shown, with fairly high consistency, that the amount of slow wave activity (delta or theta waves) in the frontal region is increased in schizophrenia. Slow wave power has been correlated with reduced blood flow and glucose utilization, and is therefore thought to reflect reduced functioning in the frontal area (Guich et al., 1989; Ingvar et al., 1976).

In UHR individuals, increased slow wave activity has been shown to predict transition to psychosis in UHR individuals in one study (van Tricht et al., 2014), but not in others (Lavoie et al., 2012). Increased frontal slow wave activity has also been associated with negative symptoms (Lavoie et al., 2012; Zimmermann et al., 2010), i.e., more severe negative symptoms was correlated with increased frontal delta power in UHR individuals who later transitioned to psychosis (UHR-P), but not in those who did not transition (UHR-NT; Lavoie et al., 2012; Zimmermann et al., 2010). Those results are in line with studies in chronic schizophrenia which have constantly shown that increased slow wave activity is correlated with negative symptoms (Gattaz et al., 1992; Guenther et al., 1988; Harris et al., 1999). More recently, increased slow wave activity in the frontal region has been associated with functional outcome in schizophrenia (Chen et al., 2016). To date, there has been no research on the association between slow wave activity and functioning, which is characteristically impaired in the UHR group.

The aims of the present study were to 1) replicate the results obtained by Lavoie et al. (2012), i.e., identify an association between increased slow wave activity in the frontal region and negative symptoms in UHR-P individuals; 2) investigate whether a similar association between increased frontal slow wave activity and poor functioning can predict transition to psychosis in UHR individuals. Our UHR population was first compared against a healthy control group in order to determine whether our UHR population showed abnormally increased frontal delta and/or theta power.

2. Methodology

2.1. Study setting

Participants were recruited from a larger pool of participants who consented to participate in the Neurapro study, a randomized controlled trial of Omega-3 fatty acids in UHR (McGorry et al., 2017). The trial's methodology has been described in detail elsewhere (Markulev et al., 2015). Full clinical assessment, including an interview with the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) to determine UHR status, and EEG recordings were conducted prior to the 6-month intervention. Transition-to-psychosis status was assessed every month during the first 6 months and then again at the 9-, 12- and 24-month follow-up, or when clinically determined using the exit criteria of the CAARMS. However, transition status is time-dependent, i.e., someone who has not transitioned at a given time-point may transition later on. Therefore, we needed a suitable timeframe to determine the UHR-P and UHR-NP cases in the present study. As the transition rate is highest during the first year (Nelson et al., 2013) and most of the individuals in our sample attended a 12-month follow-up, we used a 12-month time frame to determine the transition status. The trial was carried out at ten sites internationally, but EEG data presented in this study was collected only at the Melbourne site. 106 UHR participants were recruited from the Personal Assessment and Crisis Evaluation (PACE) clinic at Orygen Youth Health (OYH) in Parkville, Victoria and from Western Headspace in Sunshine, Victoria. The EEG side study was approved by the Melbourne Health – Human Research Ethics Committee. Written informed consent was obtained for every participant. Participation was voluntary and participants were reimbursed for their time.

2.2. Participants

Of the 106 participants (aged 15–25 years) recruited in the Neurapro study at the Melbourne site, 47 agreed to participate in the EEG side study and had their brain activity recorded at baseline, i.e., prior to commencement of treatment. Individuals were identified as being at UHR for psychosis by fulfilling one or more of the following criteria: 1) Vulnerability—individuals who have a first-degree relative with a psychotic disorder or who have a schizotypal personality disorder, 2) Attenuated Psychotic Symptoms (APS)—individuals who have experienced subthreshold, attenuated forms of positive psychotic symptoms during the past year, and/or 3) Brief Limited Intermittent Psychotic Symptoms (BLIPS)—individuals who have experienced episodes of frank psychotic symptoms that have not lasted longer than a week and have spontaneously abated. In addition to the above criteria, individuals also experienced a 30% decrease in functioning or chronic low functioning (score < 50), as indicated by the Social and Occupational Functioning Assessment Scale (SOFAS; Goldman et al., 1992), during the previous year (Yung et al., 2004). Participants were excluded if they had a past history of a psychotic episode for one week or longer, attenuated symptoms entirely explained by acute intoxication, any physical illness with psychotropic effect, intellectual disability (premorbid IQ < 70), current treatment with mood stabilizer or use of ketamine, past neuroleptic exposure equivalent to a total lifetime haloperidol dose of >50 mg, current aggression/dangerous behavior, suicidality/self-harm and pregnancy.

A group of 46 healthy controls was recruited via online advertisements or from a pool of control participants who had previously participated in research at Orygen and accepted to be approached by other researchers. Healthy controls were also aged 15–25 years old and exclusion criteria were the same as for the UHR group, with the addition of past or current mental illness.

2.3. Symptomatology and functioning assessment

Symptom severity was measured in the UHR group only. Negative symptoms were measured with the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982), depressive symptoms were assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979), severity of psychiatric symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962), was also evaluated by a psychiatrist using the Clinical Global Impression, Severity scale (CGI-S, Guy, 1976).

Functioning was assessed in both UHR and healthy controls using the Social and Occupational Functioning Assessment Scale (SOFAS;

Goldman et al., 1992), the Global Functioning (GF) scales, role (Niendam et al., 2006) and social (Auther et al., 2006), and the Assessment of Quality of Life - 8 dimensions (AQoL-8D; Richardson et al., 2014).

2.4. EEG acquisition and processing

EEG data was acquired with Neuroscan software and hardware (Compumedics, Abbotsford, Australia) and continuously sampled at 1000 Hz using a 64-site Quik-Cap (Compumedics, Abbotsford, Australia). Non-standard electrodes were placed over the left and right mastoid bones and near the eyes to measure horizontal and vertical eye movements. Each electrode was referred to an electrode placed on the nose. Resting EEG with eyes closed was recorded over 2 min, during which participants were asked to relax in a comfortable chair. A selection of evoked potentials were also measured in this study, with a rationale and hypotheses different to the current study, so the results are presented elsewhere (Lavoie et al., 2018).

EEG processing was conducted with Brain Vision Analyzer (Brain Products, Gliching, Germany). The data were referenced to the average of the mastoids. A 0.5–35 Hz phase-shift free Butterworth filter with a 24db/Oct slope was applied to the raw data. Data were segmented into 4 s long epochs that overlapped by 2 s. Epochs were then corrected for ocular movements using the Gratton et al. (1983) method. Finally, a Fast Fourier Transformation was calculated using a Hanning window of 10% taper length and normalized to 0.5–35 Hz (Kam et al., 2013). Spectral power calculated from each segments was averaged and data were exported using the following ranges: delta (0.5–4.0 Hz) and theta (4.0–8.0 Hz).

2.5. Statistical analyses

Data analyses were conducted using IBM® SPSS® Statistics Version 25. Differences in baseline characteristics of participants were assessed using Student's *t*-test for independent samples or chi-squared test as appropriate.

Multivariate Analysis of Variance (MANOVA) was used to compare the brain activity power in the delta and theta frequency bands in the frontal region between groups. Presence/absence of antidepressant medication was added as a covariate to correct for any potential effect of medication on the resting brain activity. Lateralisation was assessed using repeated-measure ANOVAs with one between-subject factors (Group: control, UHR), and one within-subject factor (Hemisphere: frontal left, frontal right; see Fig. 1 for a definition of the regions) for both frequency bands. Repeated-measure ANOVAs with one between-subject factors (Group: UHR-T, UHR-NT), and one within-subject factor (Timepoint: baseline, follow-up) were used to explore whether transition to psychosis was accompanied by a change in slow wave activity. When the assumption of sphericity was violated, the Greenhouse-Geisser correction was used.

Pearson's correlations were also conducted within each groups and sub-groups of participants to look at the association between the delta and theta power under the frontal area, and participants' scores on the SANS, MADRS, BPRS, CGI-S, SOFAS, AQoL, and the two GF scales scores.

The whole UHR group was compared to the control group to establish the baseline characteristics of the two groups, and the UHR-P subgroup was compared to UHR-NP participants to determine whether the association between symptoms/functioning and slow activity in the frontal region could differentiate between the individuals who later transitioned to psychosis from those who did not transition. Fisher r-to-z transformation was used to calculate a z-value to assess the significance of the difference between the two correlation coefficients obtained.

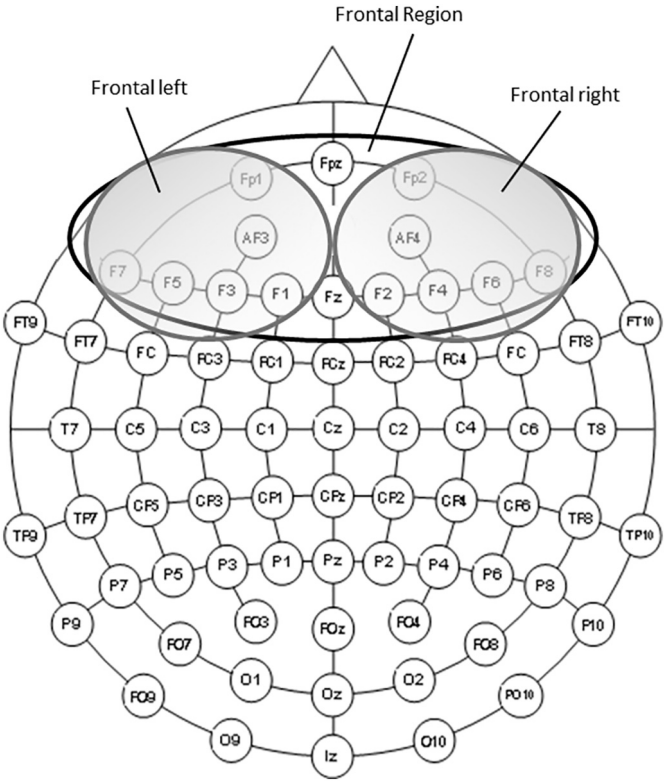

Fig. 1. Schematic representation of the Quik-Cap electrodes layout, with the definition of the three regions of interest.

3. Results

3.1. Characterization of UHR participants compared to a healthy control group

The data from eight controls and three UHR participants had to be excluded due to poor quality and, as a consequence, the number of participants in each group was 38 and 44, respectively.

Table 1
Characteristics, functional scores and resting-EEG spectral power of healthy controls and UHR individuals, as well as UHR group at intake for the UHR group only. Mean ± standard deviation unless otherwise stated.

Characteristic	Controls (n = 38)	UHR (n = 44)	p-Value
Age (years)	19.3 ± 2.2	17.8 ± 2.5	0.466[a]
Gender, nb females (%)	22 (57.9)	28 (63.6)	0.595[b]
Antidepressant medication, nb (%)	0 (0)	20 (46.5)	
At-risk for psychosis group, nb (%):			
Attenuated symptoms	–	35 (79.6)	
Trait risk factor	–	5 (11.4)	
BLIPS	–	0 (0)	
Attenuated symptoms + trait	–	4 (9.1)	
SOFAS	87.3 ± 6.3	56.9 ± 10.7	**0.001**[a]
Global functioning - social	8.9 ± 0.7	6.7 ± 1.2	**0.000**[a]
Global functioning - role	8.7 ± 0.7	6.3 ± 1.6	**0.000**[a]
AQoL	54.3 ± 9.5	99.6 ± 19.8	**0.000**[a]
EEG power (μV^2/Hz, normalized):			
Delta frontal	2.94 ± 0.88	3.10 ± 0.87	
Delta frontal left	2.95 ± 0.90	3.05 ± 0.89	
Delta frontal right	2.93 ± 0.88	3.11 ± 0.87	
Theta frontal	0.95 ± 0.32	1.12 ± 0.33	
Theta frontal left	0.95 ± 0.33	1.10 ± 0.33	
Theta frontal right	0.95 ± 0.32	1.13 ± 0.33	

Significant p-Values (<0.05) are in bold.
[a] Student's *t*-test.
[b] Chi square.

Table 1 shows that the control and UHR groups did not differ in terms of their age and gender distribution. As expected, healthy controls scored significantly higher on all four functioning scales, namely the SOFAS, both global functioning scale and the AQoL. 46.5% of UHR participants were on antidepressant medication, mainly Fluoxetine, and none of the participants were taking antipsychotic medication.

Table 1 shows the average delta and theta EEG power in the frontal region (whole region, left hemisphere, and right hemisphere) of control and UHR participants. While MANOVAs conducted on the brain activity power in the frontal region showed no difference between UHR and controls in the delta band (Pilai's trace V = 0.259, $F_{(14, 60)} = 1.502$, p = 0.138), there was a significant between-subject effect in the theta band (Pilai's trace V = 0.378, $F_{(14, 60)} = 2.600$, p = 0.005). Indeed, the EEG power in the theta frequency bands under the electrodes in the frontal region was systematically higher in the UHR group compared to the control group (Fig. 2).

Repeated-measure ANOVAs showed no Group × Hemisphere interactions, indicating no difference in lateralisation between groups.

3.2. Comparisons between UHR-P and UHR-NP

Within the 12 months of the study, eight participants had transitioned to psychosis (UHR-P). The slow wave activity of seven of them (one had to be excluded from analyses due to the poor quality of data) was compared to the 37 UHR participants who did not develop psychosis (UHR-NP) within this period, to verify whether differences in the brain activity power may predict transition to psychosis.

Table 2 shows that the UHR-NP and UHR-P groups did not differ in terms of their age, gender distribution and UHR group at intake. UHR-P showed significantly higher psychiatric symptoms than UHR-NP, as

Table 2
Demographic characteristics, UHR group at intake, symptoms and functional scores, and resting-EEG spectral power of UHR who later transitioned to psychosis (UHR-P) or not (UHR-NP). Mean ± standard deviation unless otherwise stated.

Characteristic	UHR-NP (n = 37)	UHR-P (n = 7)	p-Value
Age (years)	17.9 ± 2.7	16.8 ± 1.2	0.271[a]
Gender, nb females (%)	24 (64.9)	4 (57.1)	0.697[b]
At-risk for psychosis group, nb (%):			0.343[b]
Attenuated symptoms	28 (75.7)	7 (100.0)	
Trait risk factor	5 (13.5)	0 (0.0)	
BLIPS	0 (0.0)	0 (0.0)	
Attenuated symptoms + trait	4 (10.8)	0 (0.0)	
SANS	16.6 ± 10.6	24.4 ± **9.3**	0.076[a]
MADRS	22.4 ± 9.3	25.3 ± 6.9	0.441[a]
BPRS	41.2 ± 8.1	49.9 ± 8.1	**0.013**[a]
SOFAS	57.0 ± 10.8	56.3 ± 11.0	0.869[a]
Global functioning - social	6.7 ± 1.1	6.3 ± 1.5	0.346[a]
Global functioning - role	6.2 ± 1.6	6.6 ± 1.6	0.616[a]
AQoL	99.2 ± 20.4	N/A	
Severity of illness	3.5 ± 0.7	4.1 ± 0.7	**0.020**[a]
EEG power (μV^2/Hz, normalized):			
Delta frontal	3.13 ± 0.85	2.93 ± 1.07	
Delta frontal left	3.09 ± 0.87	2.89 ± 1.08	
Delta frontal right	3.14 ± 0.85	2.94 ± 1.08	
Theta frontal	1.11 ± 0.32	1.15 ± 0.39	
Theta frontal left	1.10 ± 0.33	1.14 ± 0.39	
Theta frontal right	1.12 ± 0.32	1.16 ± 0.40	

[a] Student's *t*-test.
[b] Chi square.

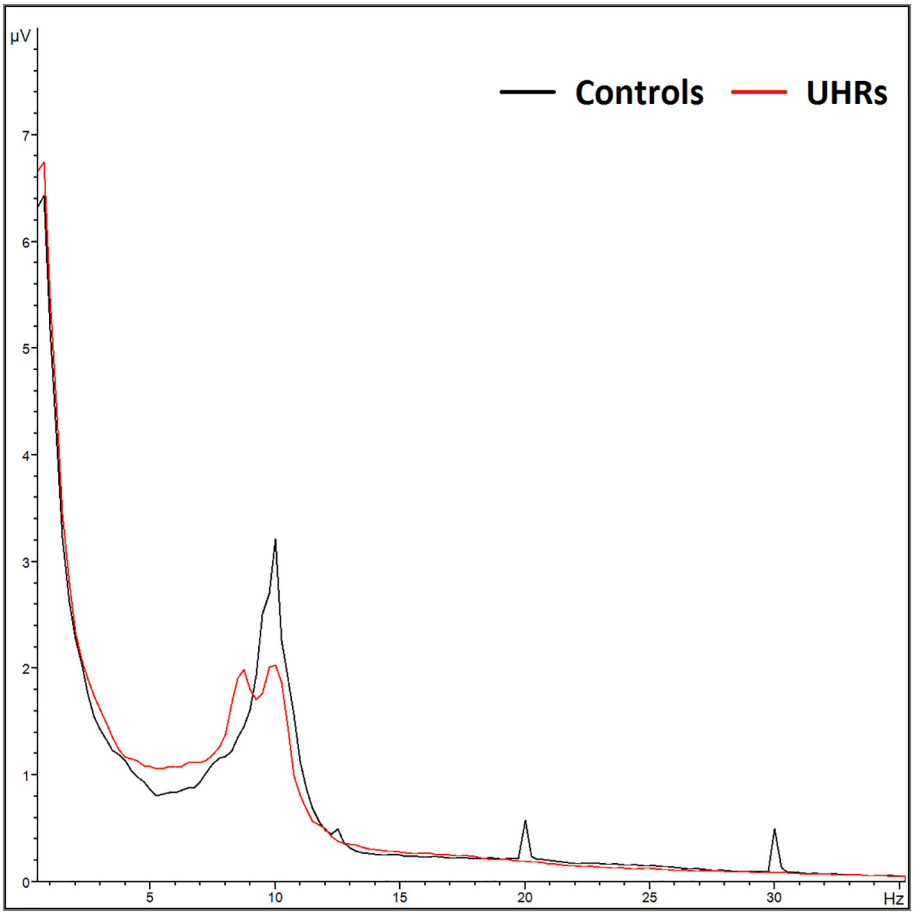

Fig. 2. Resting EEG power spectra in the control and UHR groups.

measured with the BPRS. The difference between groups in depressive and negative symptoms as measured with the MADRS and the SANS was not significant. Both UHR group showed equally impaired functioning as assessed with the SOFAS, both Global Functioning scales and the AQoL, but the UHR-P group was significantly more severely ill as assessed with the CGI-S.

MANOVAs conducted on the brain activity power in the frontal region (Fig. 1) showed no difference between UHR-P and UHR-NP in the delta band (Pilai's trace V = 0.487, $F_{(14, 27)} = 1.833$, p = 0.086) and in the theta band (Pilai's trace V = 0.313, $F_{(14, 27)} = 0.879$, p = 0.587).

Repeated measures ANOVAs showed no Group × Hemisphere interactions, indicating no difference in laterialisation between groups.

Exploratory repeated-measures ANOVAs analyses showed no Group × Timepoint interaction for both delta and theta, indicating that transition to psychosis was not accompanied by a change in slow wave activity.

3.3. Symptomology and functioning in association with slow brain activity in the frontal region

A significant positive correlation between MADRS scores and frontal delta power was observed in the UHR group (R = 0.307; p = 0.042; Fig. 3). No other significant correlations were found between symptoms and the frontal brain activity in the delta and theta frequency bands in both the control and the UHR group, as well as in the sub-group UHR-NP and UHR-P.

Regarding functioning and slow wave activity in the frontal region, no significant correlations were found in any of the groups.

4. Discussion

In the present study, an increase in the theta EEG power in the frontal region of UHR participants was measured compared to controls. However, there was no difference between groups in the delta EEG power. There was no significant difference between the UHR-P and the UHR-NP groups in slow wave power in the frontal right area. While our results showed a significant positive correlation between delta power and depressive symptoms in the UHR group, the association between delta frequency power and negative symptoms previously observed (Lavoie et al., 2012; Zimmermann et al., 2010), was not present in our UHR cohort.

Abnormalities in frontal functioning, as reflected by the increase in slow wave activity in the frontal region of the brain, are well established in schizophrenia (see meta-analysis Boutros et al., 2008b; Galderisi et al., 2009). Activity in the delta and theta bands is associated with

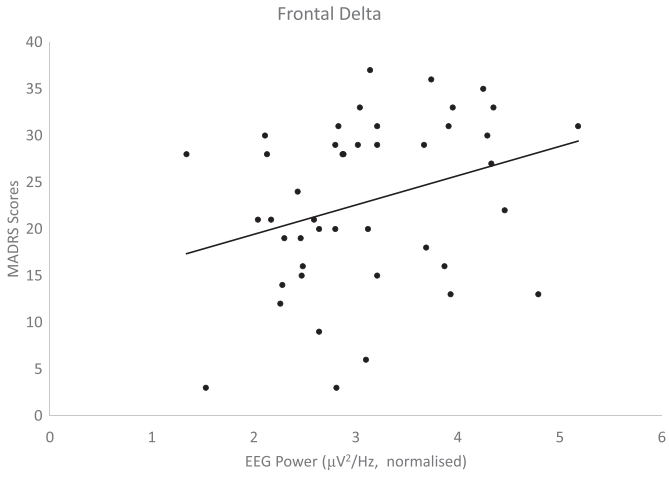

Fig. 3. The association between delta power in the frontal region and MADRS scores in UHR participants.

stages 3 and 4 of slow wave sleep (Rechtschaffen and Kales, 1968) and is potentially pathological in the waking state (Fernandez et al., 2002; Huang et al., 2012; Vieth et al., 1996), indicating some brain pathology in schizophrenia. Chronicity has a significant effect on both the delta and theta bands, with the effect size of the difference between patients and controls being much higher in chronic schizophrenia than in first-episode psychosis (FEP) patients and intermediate in mixed samples (Galderisi et al., 2009). In this study, EEG spectral power analyses performed in a UHR cohort showed higher theta power than in controls. This difference between patients and controls has repeatedly been observed in chronic schizophrenia (see meta-analyses: Boutros et al., 2008a; Galderisi et al., 2009), but not on early psychosis (Lavoie et al., 2012; Ranlund et al., 2014; van Tricht et al., 2014; Zimmermann et al., 2010). It is worth noting that our UHR sample shows higher SANS scores (17.9) compared to early psychosis samples, namely the Zimmermann et al. (about 8.5) and the Gschwandtner et al. (7.4) samples (negative symptoms were measured with the PANSS in the Lavoie et al. study). It is possible that our UHR cohort shows impaired theta activity compared to controls because they present with worse negative symptoms. Indeed, increase in slow wave activity has been associated with more severe negative symptoms in schizophrenia (Gattaz et al., 1992; Gerez and Tello, 1995; Gross et al., 2006; Sponheim et al., 2000; Venables et al., 2009) in FEP (Gschwandtner et al., 2009) and in UHR (Lavoie et al., 2012; Zimmermann et al., 2010), potentially making this association a good candidate as biomarker of the illness. However, those results were not replicated in the present study. Indeed, no association between negative symptoms and frontal slow wave activity were observed in the UHR group when compared to the control group, but more importantly, no such association was observed in the UHR-P group, weakening the argument to use this measure as a marker of the illness. It must be acknowledged, though, that the very small sample size of the UHR-P group severely limited the statistical power of this analysis, as discussed further in the limitations section.

Results are often inconsistent in UHR studies due to the high heterogeneity of the population. The Lavoie et al. (2012) cohort was a subgroup of the McGorry et al. (2017) cohort, which showed the effectiveness of omega-3 fatty acids to reduce the transition-to-psychosis rate in UHR individuals, while the current cohort was recruited from the McGorry et al. (2017) study participants, and the effects of omega-3s could not be confirmed in this larger cohort. One of the hypotheses to explain this major discrepancy between the two trials is that the sample may have been insufficiently enriched for risk of transition, with transition rates of 10.5% (McGorry et al., 2017) as compared to 16.1% in the previous study (Amminger et al., 2010). In the present sub-cohort, the transition rate was 19.5% within 12 months, which is much lower than that of the Zimmermann et al. (2010) cohort which was 46.4% within 4 years. Also, the mean age of the latter cohort (about 26 years) was higher than the present mean age of 17.8 years. Therefore, although the Zimmermann et al. (2010) cohort qualified as UHR, the fact that a higher proportion of the participants did transition to psychosis and that they were older could mean that, globally, their cohort was at a more advanced stage of the illness than the present cohort. As for the Lavoie et al. (2012) cohort, the rate of transition (24.3%) and mean age (15.7) were comparable to the present participant group. The main difference between the two studies is that negative symptoms were evaluated using two different scales, the PANSS and the SANS, respectively. It can be speculated that the negative symptoms scale of the PANSS may be more sensitive in detecting the negative symptoms that are more closely associated with the increased frontal slow wave activity. Unfortunately, the PANSS was not used in the current study, so this hypothesis cannot be verified.

In the present study, a significant association between depressive symptoms and slow wave frontal activity was rather observed. This correlation has not been commonly reported in psychosis or chronic schizophrenia. Depression has rather been associated with impaired alpha activity (for reviews, see: Olbrich and Arns, 2013; Thibodeau

et al., 2006). Although investigating the potential alpha impairment in UHR individuals was not one of the aims of the current study, visual inspection of the resting EEG spectrum reveals reduced power in the alpha frequency band. The alpha activity increases with eye closure, hence the large peek observed around 10 Hz in both groups. Apha-like waves have been associated with a variety of memory related functions (for a review, see: Klimesch et al., 2008), and research has shown that both synchrony and desynchrony of alpha waves may play a role in cognitive processes (see review by Basar and Guntekin, 2012). Our study design does not allow to verify these observations, but it appears that the alpha impairment in UHR it worth investigating.

Past studies have concluded that reduced frontal activity as indicated by the increase in slow wave activity in the frontal region, was not a good indicator of transition to psychosis (Lavoie et al., 2012; Zimmermann et al., 2010). Our results are in accordance with the literature to date with no difference between the UHR individuals who later transitioned to psychosis (UHR-P) and those who did not transition (UHR-NP) in the delta and theta frequency power in the frontal region.

To our knowledge, this is the first study to look at the association between frontal slow wave activity and functioning in a UHR population. Our results show no associations between functioning and slow wave power in the frontal region of UHR individuals when compared to controls. According to the literature, increased slow wave activity in the awake state is pathological (Fernandez et al., 2002; Huang et al., 2012; Vieth et al., 1996) and therefore, association with impaired functioning could have been expected. Although our cohort showed increased theta activity in the frontal region, this index of hypofrontality was not accompanied with worse social or role functioning, or with a decrease in quality of life.

A limitation of the current study is the small sample size, in particular for the UHR-P group, and therefore, studies in larger cohorts or meta-analyses including the present data, are granted. Another limitation is the short duration of the resting state EEG recording, as other studies in UHR participants have recorded resting EEG for at least 5 min, minimizing the noise.

5. Conclusion

Our results showed increased power in the theta band in the frontal region of UHR individuals compared to controls, but not in the delta band. Increased slow wave activity is commonly observed in psychosis, particularly in the later stages of the illness. To our knowledge, this was the first study to look at the association between frontal slow wave activity and functioning in a UHR population. Our results showed no association between functioning and the slow wave power in the frontal region of UHR individuals when compared to controls. With a small UHR-P group ($n = 8$), the power of this study is limited. Future research should be conducted to confirm if increased slow wave activity in the frontal region can predict transition to psychosis in UHR and to further investigate the disturbance in alpha activity in this population. Finding the right biomarker to add to the UHR criteria to better identify true-positives is imperative in order to minimize the duration of untreated psychosis, maximize therapeutic engagement, and consequently delay or event prevent the onset of psychosis.

Conflict of interest

The authors have no conflict of interest to declare.

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Contributions

SL designed the study, wrote the protocol and performed the statistical analyses. MS and BJ processed the data, MS drafted the manuscript. AA performed the EEG recordings. HPY gave critical advice on the statistical analyses. All authors critically reviewed the manuscript.

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