Dermatoglyphic Asymmetries, Symptoms, and Cognitive Function in Adolescents at Ultrahigh-risk for Psychotic Disorders.

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Dermatoglyphic Asymmetries, Symptoms, and Cognitive Function in Adolescents at Ultrahigh-risk for Psychotic Disorders.

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Abstract

A growing body of etiological research suggests that prenatal insult or injury can create a biological vulnerability for developing psychosis. When combined with genetic and environmental factors, these biological vulnerabilities can increase an individual’s chances of developing a psychotic disorder such as schizophrenia. One marker of prenatal insult or injury that has been widely researched in schizophrenia, but not in ultrahigh-risk (UHR) populations, is dermatoglyphics, epidermal ridge patterns that form on fingerprints and palms. Dermatoglyphics form during weeks 14-22 of fetal development, a critical time for the formation of the central nervous system (CNS). One specific neural structure that is of interest in the context of psychosis is the hippocampus, as its structure and function has been implicated across the psychosis spectrum. Further, hippocampal function is implicated in working memory deficits characteristic of individuals with psychosis, and the structure is highly sensitive during the prenatal period. In the present study, dermatoglyphics, symptoms, and cognitive data were collected on 59 UHR and 60 healthy control adolescents. The present study found elevated dermatoglyphic asymmetries within the UHR group as compared to healthy controls. No significant group differences were found in a spatial working memory task. However, elevated dermatoglyphic asymmetries were significantly associated with lower spatial working memory scores and increased attenuated symptoms but not with a more general measure of intelligence (recruiting from structures outside of the medial temporal region). The present study provides insight into prenatal vulnerabilities of a given UHR sample, and additionally supports a neural diathesis-stress model of psychosis.

Keywords: psychosis, dermatoglyphics, spatial working memory, development, hippocampus
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Psychosis is a chronic, severe, and debilitating mental illness characterized by several categories of symptoms. These include positive, negative, cognitive, and motor symptoms. Positive symptoms include strange thoughts (suspiciousness, grandiosity), sensory perceptual hallucinations (hearing or seeing things that are not there), and disorganized speech (speaking incoherently, mixing words or ideas within a sentence) (Jones, Watson, & Fone, 2011). Negative symptoms include flattened affect (reduction in facial or vocal emotional expression), alogia (decrease in spontaneous speech), and avolition (lack of motivation in certain behaviors, in particular commonly pleasurable activities such as social engagement and intimate relationships) (Jones, Watson, & Fone, 2011). Additionally, there are well-documented cognitive impairments in domains of executive functioning, attention, and memory (Velligan, Kern, & Gold, 2006). Taken together, psychotic disorders represent a heterogeneous group of mental illnesses with a wide variety of symptoms that cause impairment.

Psychotic disorders, such as schizophrenia, schizoaffective, and bipolar with psychotic features, impose a significant cost to an individual and society. Up to a total of 10% of people suffering from schizophrenia will die by suicide (Caldwell & Gottesman, 1990). In 2001, the World Health Report listed schizophrenia as the 8th leading cause of disability-adjusted life years worldwide in ages 15-44 (Wulf Rosslera, 2005). In 2002, it was estimated that schizophrenia cost the U.S. $62.7 billion, with the highest costs being due to unemployment of persons with schizophrenia (Wu, et al., 2005).
Critical to the diagnosis is that it is a deviation from the individual’s normal thoughts, moods, and behaviors (Andreasen, 1995). An individual would not have a diagnosis of schizophrenia, or any psychotic disorder for that matter, if all her or his life she or he was simply distrustful, imaginative, or eccentric. It is the change in development as well as characteristic distress and dysfunction that marks the illness (Andreasen, 1995). Schizophrenia also is not, contrary to common conceptions, a “dual” or “split” personality (Andreasen, 1995). People who have schizophrenia are not violent by nature (Walsh, Buchanan, & Fahy, 2002). Similarly, another misconception about schizophrenia is that it emerges out of “nowhere.” Schizophrenia manifests itself in phases, and current research supports this theory (Cannon, et al., 2008).

Psychosis has been associated with major impairments in brain structure and function, and this dysfunction has been a key concern recent research. These impairments have been associated with developmental disruption and are greatly impacted by stress during late adolescence and early adulthood. (Compton & Walker, 2009), (Csernansky, 2002), (Green, H. Stefef, Satz, & Christenson, 1994), (Mittal, Dean, & Pelletier, 2012). Psychotic disorders typically develop during the transition from adolescence to young adulthood, and can arrest an individual from attaining social, career and educational goals. However, research has not found a clear cause for psychosis, and therefore examining markers of abnormal brain development is critical for understanding the etiology and reasons for the disorders onset.
1.2 A neural diathesis-stress model of psychosis

At present, the exact causes of psychosis remain unknown. There is vast variability of symptom presentation within those suffering from psychosis, and it is very likely that a number of etiological processes contribute to the development of the disorder (Walker & Diforio, 1997). A diathesis stress model of psychosis suggests that genetic, biological, and neurodevelopmental abnormalities lead to vulnerability for developing the disorder. These early vulnerabilities then interact with environmental stressors during adolescence, which can lead to psychosis. Neurodevelopmental abnormalities can occur as a result of genetic inheritance as well as prenatal and obstetric complications (Mittal, Ellman, & Cannon, 2008). Psychosis is a heritable disorder as research shows that there is increased risk in individuals with family members with the disorder. Recent evidence suggests that there are several genes that might contribute greatly to risk for the disorder (Mittal, Ellman, & Cannon, 2008). For example, genes that regulate the metabolism of dopamine have been implicated because research suggests that psychosis may result from excess dopamine (Howes O. D., 2009). Evidence also suggests that genetic and epigenetic factors play a role in vulnerability (Javier Arnedo, 2015).

Prenatal insults or injury have also been associated with risk for psychosis including maternal psychosocial stress (Huttunen, 1989), prenatal exposure to viral infection (Mednick & Hollister, 1996), Rh-factor incompatibility (Hollister, Laing, & Mednick, 1996), nutritional deficiency (Susser, et al., 1996), and hypoxia (Brixey, Gallagher, & McFalls, 1993).
1.3 The ultrahigh-risk period and its interaction with early prenatal vulnerabilities

The “prodromal syndrome” is the technical term used to describe the specific group of symptoms characteristic of the ultrahigh-risk (UHR) period, and it does not qualify as any psychological or psychiatric diagnosis. It simply describes a cluster of symptoms. The ultrahigh risk (UHR) period prior to psychosis is characterized by attenuated positive symptoms as well as decreased social and role function. (Yung A. R., 2004);(Yung & McGorry, 1996). Attenuated positive symptoms have not yet reached the degree of conviction and impairment seen in formal psychosis, but may be characterized by feelings that something is “off” or increased suspicion generally. While not at the severity of formal psychosis, these attenuated positive symptoms are still jarring and concerning. Examining UHR individuals during this period is critical for preventive and intervention efforts. Indeed, early intervention may help to prevent transition or decrease its impact (Yung A. R., 2004).

Recent evidence suggests that 35% percent of UHR individuals will develop a psychotic disorder within 3 years after follow up (Fusar-Poli, 2012), (Cannon, et al., 2008), (Mittal, Saczawa, Walder, Willhite, & Walker, 2007), (Mittal, Ellman, & Cannon, 2008). Research on the biological mechanisms of psychosis may inform our understanding of etiological processes during the UHR period. Along with brain changes characteristic of healthy adolescence (Mittal, Ellman, & Cannon, 2008) (Bernard, 2014), various environmental stressors can interact with biological vulnerabilities to eventually lead to formal psychosis. These environmental stressors include sexual trauma (Thompson, 2013), drug use (Carol, 2014), and problematic family environments (Meneghelli, 2011), among others.
Psychosocial (Morrison A. P., 2012) and cognitive based (Hooker, 2014) therapies have been shown to be effective early interventions in the UHR period. New evidence suggests that exercise interventions may also help in prevention, as exercise stimulates hippocampal neurogenesis, which has been shown to help in cognitive deficits (Mittal, et al., 2013). Research shows that early intervention may be helpful in preventing the ultimate development of a psychotic disorder in UHR individuals. However, more information on the etiology of the disorder is needed in order to create more effective interventions (Morrison A. P., 2004), (Fusar-Poli P. Y., 2014).

1.4 Dermatoglyphics

A significant amount of etiological research has been focused on biomarkers, measurable features indicative of a disease, in psychosis. This includes brain imaging (Bernard, 2014), hormonal (Walker E. F., 2013), and motor variables (Dean, 2015). One class of biomarkers that may reflect disruptions in early fetal development includes minor physical anomalies in the face, hands, and feet (Ismail, Cantor-Graae, & McNeil, 2000). Dermatoglyphics are the epidermal ridge patterns that form on fingerprints and palms during weeks 14-22 of fetal development, a critical time for the formation of the central nervous system (CNS) (Compton & Walker, 2009). Examining dermatoglyphics provides a physical representation of possible CNS impairment, and may be important for the assessment of risk for psychosis. Researchers in fields of forensic psychology have developed methods to examine dermatoglyphics by counting the ridges between distinct structural formations on the fingertips and palm of the hand (i.e., triradius; or the area in which three ridge lines converge in a unique pattern).
1.5 The role of the HPA axis and the hippocampus in schizophrenia

One of the leading hypotheses about which brain areas might be responsible for the illness is the dopamine (DA) hypothesis. Breier, Davis et al. (1993) and Wolkowitz, Doran, Breir, Roy and Pickar (1989) each conclude that schizophrenia patients show more pronounced DA release than other psychiatric patients.

Stress plays a large role in the etiology of psychosis and there is a large amount of research to suggest that areas of the brain that regulate the stress response, including the hippocampus, hypothalamus, and pituitary gland may be impaired in psychosis (Walker, Mittal, & Tessner, 2008). The hypothalamic-pituitary-adrenal (HPA) regulates cortisol secretion, a primary stress hormone. In response to stress, the HPA axis increases the level of cortisol in order to control sympathetic and parasympathetic nervous system response to stress. The hippocampus is believed to play an important role in the feedback system that serves to modulate the activation of the HPA axis (Walker & Diforio, 1997) (Walker, Mittal, & Tessner, 2008).

Constant exposure to stressors can cause permanent changes to the HPA axis. In particular, a negative feedback system that mediates HPA activation may be damaged (Sapolsky, 1992), (Sapolsky R. M., 1990), (Sapolsky R. K., 1985), (Sapolsky R. &., 1990), (Stein-Behrens, 1994). As noted, prenatal insult and genes play a role in abnormal neurodevelopment in psychosis, and this may be particularly relevant to the HPA axis and the stress response. In adolescents at risk for psychosis, there are observations of increased cortisol during rest, suggesting an inability to turn off the stress response.
Increased stressors may play a role in damaging the hippocampus. Additionally, increased stress is thought to impair cognitive functions associated with hippocampal functioning such as spatial working memory. Spatial working memory is the process that allows an individual to temporarily process and store information about one’s environment and spatial orientation (Ang & Lee, 2008). Impairment in spatial working memory may lead to impairments in everyday functioning, such as schoolwork and fluently navigating directions. It is important to look at hippocampal function not only as a marker of general spatial working memory dysfunction, but also as a marker of increased stress response. Hippocampal function is of unique concern in UHR individuals, as it sheds light on general daily functioning as well as more specific structural abnormalities possibly due to prenatal insult or injury as well as stress.

1.6 Statement of purpose

Self report methods of examining prenatal insult and obstetric complication may be vulnerable to over-reporting or recall bias. Dermatoglyphics contrast with other measures of developmental insult or injury, such as self-report obstetric complications or even hospital records, because they occur on a continuum, and in a continuous fashion across the normal population (Holt, 1958). Dermatoglyphics are also not prone to a recall bias associated with self-reports of pregnancy complications, providing reliable information of obstetric complications. Further, the timing of epidermal ridge formation limits potential contributing factors to the early prenatal period, when the outer layer of the embryo (i.e., ectoderm) forms both the skin and the central nervous system (CNS) (Compton & Walker, 2009).
The hippocampus may play a role in spatial working memory (Logie, 2014) (Sanderson & Bannerman, 2012), (Heckers, 2001), (Aggleton, Hunt, & Rawlins, 1986) (Galea, Ormerod, Kostaras, Wilkie, & Phelps, 2000). In addition to regulating the biological stress response, psychosis researchers are also interested in the hippocampus because it contributes to critical aspects of cognitive functioning such as spatial working memory (Lee & Kesner, 2002), a domain also found to be impaired in schizophrenia and UHR states (Glahn, et al., 2003). If certain prenatal environments damage the hippocampus, individuals expressing increased exposure to prenatal insult or injury ought to also show a decrease in spatial working memory task scores. Given the importance of the hippocampus in the development and course of schizophrenia, and given it is uniquely sensitive during the prenatal period, it is relevant to examine the relationship between a hippocampal spatial memory task in order to see if there are relationships between symptoms, dermatoglyphic asymmetries, and spatial memory. I hypothesized that UHR participants will have increased average ridge differences when compared to healthy controls and dermatoglyphic asymmetries will be associated with positive and negative symptom domains. In order to examine the relationship between dermatoglyphic asymmetries and cognitive function tied to hippocampal impairment, I hypothesized that UHR participants will show lower cognitive scores on spatial span task than healthy controls and greater dermatoglyphic asymmetries will be related to spatial memory impairment.

2. Methods

2.1 Participants
Participants were recruited at the Adolescent Development and Preventive Treatment (ADAPT) research program. A total of 119 participants (n= 59 UHR, 60 Control) between the ages of 12 and 21 (Mean age = 18.33, SD = 2.29) were recruited by Internet advertising, email postings, newspaper ads, and community professional referrals. Exclusion criteria included history of head injury, the presence of a neurological disorder, lifetime substance dependence, and the presence of any contraindication to the magnetic resonance imaging environment. The presence of an Axis I psychotic disorder was an exclusion criterion. The presence of a psychotic disorder in a first-degree relative or meeting for an Axis I disorder was an exclusionary criterion for controls. The university institutional review board approved the protocol and informed consent procedures.

2.2 Procedure: Clinical interviews

UHR individuals met criteria for a UHR or prodromal syndrome based on the Structured Interview for Prodromal Syndromes (SIPS) criteria: 1) recent onset or escalation of moderate levels of attenuated positive symptoms, 2) a decline in global functioning over the last 12 months accompanying the presence of schizotypal personality disorder, 3) a decline in global functioning over the last 12 months accompanying the presence of a first-degree relative with a psychotic disorder such as schizophrenia.

The Structured Clinical Interview for Axis-I DSM-IV Disorders (SCID) (First, 2012) was also administered to rule out a psychotic disorder diagnosis. This measure has been demonstrated to have excellent inter-rater reliability in adolescent populations.
(Lobbestael, 2011) and has been used in several previous studies focusing on adolescent populations with schizophrenia spectrum disorders (Howes, 2009).

2.3 Dermatoglyphics

Dermatoglyphic asymmetry was assessed for homologous fingers of the right and left hands of the participants. Fingerprints were obtained by utilizing digital scans of the actual hand from a high-definition photo scanner (Epson Perfection V500 Photo Scanner). Coders rated each of the dermatoglyphics by using Adobe Photoshop (CS3), which allowed high-level zoom/enlargement and demarcation. Because of this technology, the prints were of very high quality, and consequently it was not necessary to code partial prints or use subjects with missing fingers due to poor print quality. Employing a widely adopted procedure described by Holt (Holt, 1958), the number of dermal ridges crossing a line drawn between the center of the pattern (core) and the triradius of each fingerprint was counted for all fingers on both hands. The number of ridges on each finger of the left hand was subtracted from the number of ridges on the homologous finger of the right. The total ridge count asymmetry score was calculated by summing the absolute values of the differences observed for each homologous finger pair, and taking the mean for each participant (i.e., the total discrepant ridge count divided by five). Raters trained by practicing on sets of handprints for a one-month period, and continued until intra-class correlation coefficients (ICCs) > .80. Quality is periodically assessed by a gold standard rater.

2.4 Cognitive Tasks
A subsection of 103 participants (UHR n = 52, control n = 51) were administered the Word Reading subtest of the fourth edition of the Wide Range Achievement Test (WRAT) as a measure of general intelligence. The WRAT is a well-validated and broadly used measure of achievement and broad learning ability for adolescents and young adults (Wilkinson & Robertson, 2006). Participants were asked to read 15 letters and 55 words. The total number of letters and words read correctly is transformed into a standard score normed for each age group.

A subsection of 112 participants (UHR n = 55, control n = 57) were also administered a subtest of the Weschler Memory Scale-Third Edition (WMS-III), a highly reliable, well-validated and broadly used spatial memory task battery. Scores can be interpreted based on norms on a scale relative to an individual’s age (The Psychological Corporation, 1997). The WMS-III Spatial Span test consists of a three-dimensional display of blocks with numbers on each block only visible to the examiner. The examiner taps a sequence, and the participant must tap the same sequence after the fact.

2.5 Statistical strategy

Independent samples $t$-tests and chi-square tests were employed to examine differences in continuous and categorical demographic variables between groups. Independent samples $t$-tests were used to examine group differences in target variables, including average ridge differences, and WRAT and WMS-III uncorrected $t$-scores. Bivariate correlations were also used to examine predicted relationships between dermatoglyphic asymmetries, symptoms, and cognitive task scores. Correlations were
first run with the entire sample and then in the UHR group alone in order to examine if results were unique to the UHR group.

3. Results

3.1 Participants

A total of 119 (59 UHR, 60 control) adolescents participated in a study of symptoms, epidermal ridge count asymmetries, and cognitive task scores. As reported in Table 1, no significant differences were reported in demographic characteristics such as age, gender and parental education. As expected, UHR participants were rated significantly higher than controls on all three SIPS symptom domains positive t(117)=19.7, \( p \leq .001 \), negative t(117)=10.6, \( p \leq .001 \), and disorganized t(117)=11.3, \( p \leq .001 \)

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Insert Table 1
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3.2 Group differences in dermatoglyphics and cognitive variables

The UHR group showed significantly elevated dermatoglyphic asymmetries than healthy controls, \( t(117) = 2.42, p \leq .05 \). The UHR group did not show significantly worse scores on the spatial span task compared to healthy controls. There were no significant group differences using the WRAT between UHR and healthy control \( t(101) = 1.48, p = .14 \).
3.3 *Relationship between dermatoglyphic asymmetries and symptoms*

In order to investigate the relationship of dermatoglyphic asymmetries to positive, negative, and disorganized symptoms, one-tailed bivariate correlations were examined for the entire sample and within the UHR group. Across the entire sample \( (n=119) \), higher average ridge differences were related to elevated positive symptoms \( r(117) = .16, p \leq .05 \), elevated negative symptoms \( r(117) = .17, p \leq .05 \), and elevated disorganized symptoms \( r(117) = .19, p \leq .05 \). All between-group relationships were statistically significant. Within the UHR and control groups alone, however, there were no significant relationships between dermatoglyphic asymmetries and positive, negative, or disorganized symptoms.

3.4 *Relationships between dermatoglyphic asymmetries and cognitive tasks.*

In order to examine the relationship between dermatoglyphic asymmetries to the various cognitive tasks, one-tailed bivariate correlations were examined for the entire sample and within the UHR group. Across the entire sample, higher average ridge differences were significantly related to lower spatial working memory scores, \( r(110) = -.18, p=.03 \). Within the UHR sample \( (n=55) \), higher ridge differences were significantly related to lower scores in spatial working memory, \( r(53) = -.30, p=.01 \). No significant
4. Discussion

Consistent with past research on dermatoglyphic asymmetries in schizophrenia samples (Reilly, Murphy, & Byrne, 2001), the present study found significant group differences in ridge count asymmetries in a UHR compared to healthy controls. The results suggest a relationship between positive, negative and disorganized symptoms and dermatoglyphic asymmetries, possibly reflecting an impaired neurodevelopment contributing to the development of these symptoms. The findings of increased dermatoglyphic asymmetries and spatial working memory may indicate impairment to brain regions important for cognitive function, including the hippocampus, a structure heavily implicated in the etiology of psychosis. Finally, the results are consistent with a neural diathesis stress model, which suggests that minor physical anomalies are present from birth and may be linked to core symptom and cognitive functioning in UHR individuals.

4.1 Dermatoglyphic asymmetries in various samples

Dermatoglyphic asymmetries have been found in several samples across the schizophrenia spectrum. On one end of the continuum, researchers have found dermatoglyphic asymmetries in a sample reporting non-clinical psychosis (NCP) (Mittal, Dean, & Pelletier, 2012). Similarly, asymmetries have been found in samples with those
suffering from schizotypal personality disorder (SPD) (Mittal, Dhruv, Tessner, Walder, & Walker, 2007). Several studies have shown the presence of dermatoglyphic asymmetries in schizophrenia samples. Markow and Wandler were among some of the earlier researchers who found significant group differences in dermatoglyphic asymmetries between individuals with schizophrenia and healthy controls. (Markow & Wandler, 1986). Markow and Gottesman suggest that their findings of fingerprints of concordant and discordant twin pairs support a genetic prediction (Markow & Gottesman, 1989). Yet another study among many also found group differences in dermatoglyphic asymmetries between individuals suffering from schizophrenia and healthy controls (Mellor, 1992). Reilly et al. found group differences between patients with schizophrenia and controls in regards to dermatoglyphic abnormalities and atypical handedness (an established marker of developmental insult) (Reilly, Murphy, & Byrne, 2001).

Early research indicated that there may not have been a relationship between dermatoglyphic abnormalities and prenatal viral infection, nutritional deficiency, and hypoxia (Walker & Diforio, 1997). However, more recent studies have shown that hypoxia can be related to eventual development of a psychotic disorder (van Erp, 2014). Another study showed elevated dermatoglyphic asymmetries in children born from mothers who experienced a natural disaster during pregnancy (King, Mancini-Marie, Brunet, Walker, Meaney, & LaPlante, 2009). While some studies have found differences in dermatoglyphic asymmetries; it is still unclear if dermatoglyphics are related to eventual transition to psychosis. Future work examining the relationship of dermatoglyphics to eventual transition to psychosis is sorely needed to clarify this important issue.
4.2 *Dermatoglyphic asymmetries and symptoms*

Several studies have noted relationships between dermatoglyphics and symptoms of psychosis. As predicted, the present study found significant relationships between dermatoglyphic asymmetries and positive symptoms. This relationship could reflect an association between prenatal disruption and the eventual development of positive symptoms. Dermatoglyphics reflect impaired neurodevelopment, and environmental stressors during the UHR period could lead to the evolution of psychosis when combined with constitutional vulnerabilities. The present study also found significant relationships between dermatoglyphic asymmetries and negative symptoms. The present study did not find significant results within the UHR group alone with regards to dermatoglyphic asymmetries and symptoms. However, this could simply be a result of statistical power. The narrow variability of the small UHR sample alone could have affected these results. Given the significant results of the entire-sample correlations, more studies with larger UHR sample sizes ought to be conducted as follow-up in order to examine if dermatoglyphics are related to symptoms. The category of symptoms with the strongest relationship to dermatoglyphic asymmetries was disorganized symptoms. At present, there is no known research distinguishing between different categories of symptoms and their relationship to prenatal insult or injury. However, it is notable that in this sample, disorganized symptoms have the strongest relationship to dermatoglyphic asymmetries. There are several reasons for this, including the fact that disorganized behavior often involves daily functioning. Perhaps, within the context of this daily functioning, skills involving spatial working memory may be implicated, such as remembering directions,
or where one left an important document (Logie, 2014). The present study does not claim to be able to make connections between dermatoglyphic asymmetries and disorganized symptoms (with regards to their relationship to spatial working memory), but the findings suggest a potential area of further research within this context.

4.3 Dermatoglyphic asymmetries and cognitive ability

The current findings suggest that there may be a trend in regards to relationships between dermatoglyphic asymmetries and decreased performance on the spatial working memory tasks. While it was predicted that there would be group differences in spatial span tasks, the results suggest that there may be a relationship between increased dermatoglyphic asymmetries and impaired spatial working memory. Weinstein et al. (1999) acknowledged the presence of cognitive deficits as a marker of the illness in their examination of dermatoglyphic asymmetries and cortisol in SPD, but did not run analyses including cognitive tasks in their investigation of dermatoglyphic asymmetries and symptoms (Weinstein, Diforio, Schiffman, Walker, & Bonsall, 1999). The present study fills a gap in this research, connecting a marker of prenatal insult and injury, dermatoglyphic asymmetries, to prodromal symptoms and their characteristic cognitive deficits.

In Mittal et al.’s study on dermatoglyphics in non-clinical psychosis, the authors found group differences in regards to dermatoglyphic asymmetries and relationships between asymmetries and symptoms, but they also found significant relationships between these scores and procedural learning deficits. Procedural learning is believed to be related to fronto-striatal function (Mittal, Dean, & Pelletier, 2012). One study looking
at minor physical anomalies (MPAs), a broader category of phenotypic representation of prenatal insult, in schizophrenia (Ismail, Cantor-Graae, & McNeil, 2000) found no significant associations between MPAs and cognitive dysfunction. According to the authors, these results suggest that MPAs are possibly markers of aberrant neurodevelopment (Ismail, Cantor-Graae, & McNeil, 2000).” In contrast, the advantage of the present study is that it examined the relationship between one specific MPA, dermatoglyphics, and related it to a cognitive task associated with the hippocampus. Taken together, results supported the hypotheses that dermatoglyphic asymmetries may be linked to a hippocampal dependent cognitive function. These findings have significant ramifications for informing future research in this area, which should incorporate a broader battery focusing on early prenatal insult, and a more widespread range of hippocampal functions.

4.4 Present findings and the Diathesis-Stress Model

The Diathesis-Stress Model suggests that genetic, biological, or neurodevelopmental abnormalities lead to vulnerability for developing schizophrenia or other psychotic disorders. These early vulnerabilities then interact with environmental stressors, which can lead to psychosis. The present study provides a window into a given time in the prenatal period that relates to symptomology and spatial working memory deficits during adolescence and young adulthood, when stressors are increasing and the risk for psychosis is greater. Importantly, this study found that cognitive functions tied to brain regions implicated in the pathophysiology of psychosis are related to dermatoglyphic asymmetries.
4.5 Limitations and future directions

The current study has several noteworthy strengths. However, it could be improved upon in several ways. First, while the sample size is comparable to other studies in at-risk and schizophrenia populations (Mittal, Dean, & Pelletier, 2012) (Mittal, Dhruv, Tessner, Walder, & Walker, 2007) (Cannon, et al., 2008), a larger sample may provide more opportunity to investigate the relationship between dermatoglyphic asymmetries and cognitive impairment. In a related point, the current study examined spatial working memory, however, other research suggests that UHR individuals are impaired in several other domains. Future work to examine multiple cognitive domains in relationship to dermatoglyphics may provide a clearer picture of the relationship between signs of altered neurodevelopment and cognitive impairment prior to the onset of psychosis. The current study examined dermatoglyphics, symptoms and spatial working memory during one time point, however, examining the relationship to symptoms and cognitive function over multiple time points may provide important information regarding the predictive utility of these dermatoglyphic asymmetries as psychosis develops. Finally, dermatoglyphics are thought to be one marker of CNS development, specifically reflecting hippocampal impairment. It will be important for future work utilizing several indices of minor physical anomalies and multimodal imaging to investigate structural and functional relationships between dermatoglyphic asymmetries to other brain regions in order to get a clearer picture of how dermatoglyphics are related to the altered neurodevelopment characteristic of psychosis.
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Table 1. Group differences in demographics, symptoms, dermatoglyphics and cognitive tasks

<table>
<thead>
<tr>
<th></th>
<th>Ultrahigh-Risk</th>
<th>Healthy</th>
<th>Differences</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean years (S.D.)</td>
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<td>18.02(2.7)</td>
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<td><strong>Gender</strong></td>
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<td>32</td>
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<tr>
<td>Female</td>
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</tr>
<tr>
<td>Total</td>
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<tr>
<td><strong>Parent education</strong></td>
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<tr>
<td>Mean years (S.D)</td>
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<td>15.65(2.3)</td>
<td>N.S.</td>
</tr>
<tr>
<td><strong>SIPS scores</strong></td>
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<td>Positive symptoms</td>
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<tr>
<td>Mean (S.D)</td>
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<td>Negative symptoms</td>
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</tr>
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<td>Disorganized symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D)</td>
<td>5.61(3.6)</td>
<td>.27(.69)</td>
<td>p≤.001</td>
</tr>
<tr>
<td><strong>Dermatoglyphics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Ridge Differences</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>2.7 (1.8)</td>
<td>1.9(1.5)</td>
<td>p ≤ .05</td>
</tr>
<tr>
<td><strong>Cognitive tasks</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WRAT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>109.29 (13.0), n=52</td>
<td>105.14 (14.4), n=51</td>
<td>N.S.</td>
</tr>
<tr>
<td>Spatial span</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>54.7 (10.5), n=55</td>
<td>54.9 (9.3), n=57</td>
<td>N.S.</td>
</tr>
</tbody>
</table>
### TABLE 3. Whole Sample Associations Between Dermatoglyphic Asymmetries, Cognitive Task Scores, and Symptoms

<table>
<thead>
<tr>
<th>Domain</th>
<th>Average Ridge Differences</th>
<th>Spatial Span</th>
<th>General Intelligence</th>
<th>Positive Symptoms</th>
<th>Negative Symptoms</th>
<th>Disorganized Symptoms</th>
</tr>
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<td>Average Ridge Difference</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Spatial Span Test</td>
<td>-.183*</td>
<td>.010</td>
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<tr>
<td>Word Reading Subtest</td>
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<td>-.029</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Positive Symptoms</td>
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<td>-.016</td>
<td>.158</td>
<td>.164*</td>
<td>.158</td>
<td>.736**</td>
</tr>
<tr>
<td>Negative Symptoms</td>
<td>.174*</td>
<td>-.164*</td>
<td>.047</td>
<td>.047</td>
<td>.736**</td>
<td>.795**</td>
</tr>
<tr>
<td>Disorganized Symptoms</td>
<td>.192*</td>
<td>-.148</td>
<td>.058</td>
<td>.814**</td>
<td>.795**</td>
<td>1</td>
</tr>
</tbody>
</table>
### TABLE 4. UHR Sample Associations Between Dermatoglyphic Asymmetries, Cognitive Task Scores, and Symptoms

<table>
<thead>
<tr>
<th>Domain</th>
<th>Average Ridge Differences</th>
<th>Spatial Span</th>
<th>General Intelligence</th>
<th>Positive Symptoms</th>
<th>Negative Symptoms</th>
<th>Disorganized Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Ridge Difference</td>
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</tr>
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<td>Spatial Span Test</td>
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<td>-.059</td>
<td>1</td>
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</tr>
<tr>
<td>Positive Symptoms</td>
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<td>-.016</td>
<td>.065</td>
<td>.065</td>
<td>-.277*</td>
<td>.354**</td>
</tr>
<tr>
<td>Negative Symptoms</td>
<td>.067</td>
<td>-.277*</td>
<td>-.123</td>
<td>.354**</td>
<td>.537**</td>
<td>.582**</td>
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<tr>
<td>Disorganized Symptoms</td>
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<td>-.279*</td>
<td>-.107</td>
<td>.537**</td>
<td>.582**</td>
<td>1</td>
</tr>
</tbody>
</table>
Figure 1. Relative lifetime prevalence of schizophrenia (British Columbia Schizophrenia Society, 2013)
Figure 2. The Diathesis-Stress Model, as conceptualized by Walker and Diforio (Walker & Diforio, 1997).
Figure 3. Asymmetrical dermatoglyphic patterns. In this example of an asymmetrical print pair, taken from a non-participant model, the ridge count between the triradius (meeting of patterns on the periphery of the print) and core (center of print) for the left finger L3 (a) is markedly higher than that of the corresponding homologous right finger R3 (b) (Mittal, Dean, & Pelletier, 2012).
Figure 4. The WMS-III spatial span assessment. (The Psychological Corporation, 1997)
Figure 5. WRAT scores across the entire sample, showing non-significant relationships across the sample.
Figure 6. WMS-III scores across the entire sample, showing significant correlations between increased ridge differences and decreased spatial span scores.