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REVIEW

DERMATOGLYPHICS – A POSSIBLE BIOMARKER IN THE NEURODEVELOPMENTAL MODEL FOR THE ORIGIN OF MENTAL DISORDERS

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ДЕРМАТОГЛИФЫ – ВОЗМОЖНЫЙ БИОЛОГИЧЕСКИЙ МАРКЕР В НЕЙРООНТОГЕНЕТИЧЕСКОЙ МОДЕЛИ ПРИ ВОЗНИКНОВЕНИИ ПСИХИЧЕСКИХ ЗАБОЛЕВАНИЙ

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ABSTRACT

Introduction: Dermatoglyphic pattern formation and differentiation are complex processes which have been in the focus of research interest ever since dermatoglyphics became a science. The patterns' early differentiation and genetic uniqueness as well as the relatively simple methods used to obtain and store fingerprints make it possible to study the relationship between certain dermatoglyphic characteristics and the underlying pathological processes in a number of diseases, including mental disorders. **Aim:** The present review reports published data from fundamental and clinical studies on dermatoglyphics primarily in schizophrenia and bipolar disorder to lend additional support for the neurodevelopmental hypothesis in the etiology of these disorders. Following an analysis of the theories of dermatoglyphics formation and the complex association between ridge patterns and central nervous system in early embryogenesis, an attempt is made to present dermatoglyphics as possible biological markers of impaired neurodevelopment. **Conclusions:** The contradictory data in the literature on dermatoglyphics in mental disorders suggest the need for further studies on these biological markers in order to identify their place in the neurodevelopmental etiological model of these diseases.

Key words: *dermatoglyphics, biomarkers, schizophrenia, neurodevelopment*

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РЕЗЮМЕ

Введение: Образование и детерминирование индивидуального дерматоглифического рисунка представляет собой сложный процесс, волнующий исследователей еще со времени возникновения дерматоглифики как наука. Ранняя дифференциация папиллярных отпечатков, (признак индивидуальности) и сравнительно нетрудные методы получения и сохранения отпечатков, дают возможность надежно исследовать дерматоглифы, а также и поставить себе целью найти их связь с определенными характеристиками при ряде заболеваний, в том числе и при психических расстройствах. **Цель:** Настоящий обзор знакомит с литературными данными ряда клинических и теоретических исследваний дерматоглифических признаков преимущественно при шизофрении, подкрепляя нейроонтогенетическую гипотезу развития психических заболяваний. После анализирования теорий формирования папиллярных рисунков и сложных взаимоотношений между папиллярными изображениями и центральной нервной системой во время ранних периодов их эмбрионального развития сделан опыт представить дерматоглифы как возможный биологический маркер нарушенного развития. **Заключение:** Наличие противоречий в дермотоглифической характеристике при психических расстройствах, о которых свидетельствуют многие литературные данные, указывает на необходимость в дополнительных исследованиях этих биологических маркеров с целью установить их место в нейроонтогенетической модели возникновения этих заболеваний.

Ключевые слова: *дерматоглифика, биомаркеры, шизофрения, нейроонтогенез*

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INTRODUCTION

Dermatoglyphic pattern formation and differentiation are complex processes occurring at the boundary between epidermis and dermis with a possible correlation with hand and foot development. The precise mechanisms of ridge configuration and the factors influencing this process have been exciting researchers' interest since dermatoglyphics became a science. The patterns' early differentiation and genetic uniqueness as well as the relatively simple methods to obtain and store fingerprints make it possible to study the relationship between certain dermatoglyphic characteristics and the underlying pathological processes in a number of diseases, including mental disorders.[1,2] Deviations in the dermatoglyphic patterns have been described in sickle cell anemia, psoriasis, epilepsy, tumors, congenital heart disease, lupus erythematodes, mental disorders. Dermatoglyphic studies in children with visual, hearing and intellectual impairment are also of great interest.[3] The specific ridge pattern examination has become almost a routine procedure in the diagnosis of the number and structure variations of chromosomes in polygenetic and chromosomal disorders.[4]

Over the last years a tendency of using biological markers in mental disorders has been observed, focusing on early prenatal brain damages and caused by the influence of a certain static agent. In this sense ridge patterns might become reliable biomarkers for neurodevelopmental disorders, which is assumed in the neurodevelopmental hypothesis of mental disorders. Prerequisites for the utility of dermatoglyphics are the complex phases of embryonic morphogenesis and the factors affecting the differentiation of the ridge patterns.

THEORIES OF DERMATOGLYPHIC FORMATION

The first hypotheses for papillary pattern formation were advanced in the studies of Kollmann and Bonnevie, where the effect of different forces of pressures and tensions determining the primary ridge development was suggested.[5] In a 1924 study, Bonnevie reported that the basal epidermal cells were exposed to mechanical compression forces because of their rapid proliferation. It was these stress effects that directed the cells towards the soft underlying dermis, which resulted in the formation of the primary ridges. This theory was later popularised by Harold Cummins, who argued that there was a connection between hand geometry and ridge patterns and that this connection was established by growth forces acting on the fetal skin.[6] Although rejected by most authors, this theory became a basis for the subsequent research which is still being conducted in the present years.

Kücken proposed a mathematical model to demonstrate the impact of stress factors on the development of specific ridge geometry of the hands and feet.[7] In 2013 Kücken and Champod elaborated the suggested mathematical model by testing the role of Merkel cells.[8] The authors assumed that ridge direction could be determined by the areas of greater stress during the interaction of Merkel cells with one another and with these dermal regions. Merkel cells might be directed towards the most significant forces of tension, which could define the location of the volar ridges.

Many studies support the idea of a relationship between dermatoglyphics and the nervous system, particularly between the pattern type and the branching of the peripheral nerves and blood vessels.[9] What these studies basically suggest is that ridge patterns correspond to the course of capillary and nervous network underneath. Although there is obviously an association between the development of the nervous system and the dermal ridges, conditioned by their common ectodermal origin, volar topography cannot be explained only with the nerve branching, especially regarding the complex dermatoglyphic patterns such as whorls and loops.[7]

The fibroblast hypothesis for the formation of dermatoglyphic patterns implies the involvement of fibroblast cells which have the ability to generate significant tensile forces, affecting the extracellular matrix and the formation of epidermal ridges.[10] A disadvantage of this hypothesis is that there is no clear evidence of an association existing between fibroblasts and finger ridge patterns.

Most of the researchers also do not exclude the hypothesis that ridge patterns are genetically determined and hereditary in nature. As early as in 1946 Harold Cummins defined some characteristics of the dermatoglyphic patterns as hereditarily determined: these are the type of the pattern (whorl, loop, arch), and the size of the pattern as determined by the number of ridges composing it.[11] Cummins argued that the inheritance of these signs was dependent upon a number of factors that are less rigidly controlled, as evidenced by the differences in dermatoglyphic patterns in monozygotic twins. Ridge patterns of such twin pairs are never completely identical, as the regulatory mechanisms of their inheritance cannot be totally controlled. During the process of pattern differentiation or even before the final formation of the ridges, circumstances beyond hereditary control may affect

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the configuration of the dermatoglyphic model. The formation of the smallest details is certainly not hereditarily controlled, but even the basic features of papillary pattern can be inhibited although they are genetically determined resulting in the appearance of an entirely different final pattern. This is relatively better manifested in the dermatoglyphic patterns of the feet where the patterns are subject to a less hereditary control than the ridge patterns of the hands. This phenomenon is supported by the significant differences in the papillary ridges of the feet identified in monozygotic twin pairs.[11] Although the genetics of volar ridge topography is undoubtedly involved in the process it is still not completely explained.

DERMATOGLYPHICS AND NEURODEVELOPMENT

The significance of dermatoglyphics as biological markers of abnormal neurodevelopment in mental disorders is associated with the common embryonic origin of the brain and the papillary patterns. The morphogenesis of the dermal ridges occurs simultaneously with the formation of the midline brain structures of the same ectodermal origin. There are many imaging studies of the brain that have found replicable structural abnormalities in schizophrenia and bipolar disorder manifested by significant loss of gray matter, increased ventricular space and pathological changes in the prefrontal and medial temporal cortex.[12,13] The causes of abnormal dermatoglyphic status in the presence of morphological brain impairment in mental disorders might be found in the early stages of embryogenesis.

Ridge patterns appear on the pads of the fingers, interdigital areas, thenar and hypothenar of the palms and soles.[14] This process starts in 6.5 gestational weeks, first in the palms of the hands, a week later in the fingertips, and finally in the soles of the feet. Between 6.5 and 10.5 weeks, volar pads exhibit rapid growth and by 9 weeks they begin to differentiate in shape and position.[15] Simultaneously with these processes, there occurs a rapid growth of the brain hemispheres which develop at about 6.5 gestational weeks. At the end of the IV embryonic month human fetus acquires epidermal ridge configuration comparable to that of an adult, while the main departments of the central nervous system are almost entirely developed. A critical period in the differentiation of ectodermal derivatives is the III embryonic month when different exogenous factors may distort the normal differentiation of epidermal ridges resulting in morphological brain abnormalities. Once developed, the ridge patterns remain unchanged throughout postnatal life, even after superficial dermal injuries.[15] Because of the long latent period in the development of mental disorders, brain structural abnormalities may be found in imaging studies of patients long after the alleged impact of exogenous agent. In this sense, the common embryonic origin of papillary ridges and brain structures, as well as the strictly defined periods of formation, may designate dermatoglyphics as potential extracranial biomarkers in determining the time of impact of the prenatal agent.

FINGER DERMATOGLYPHICS IN MENTAL DISORDERS

The majority of published data on finger dermatoglyphics in mental disorders comprise comparisons between patients with schizophrenia and mentally healthy controls.[16,17] Research on dermatoglyphics in bipolar disorder is scanty, although the two disorders share some common clinical and epidemiological features. Some authors have found a reduced frequency of whorls and an increase of loops in male patients with schizophrenia compared with healthy men.[18,19] Some studies have found an increase in the whorls in schizophrenic males and in the arches in schizophrenic females with the gender differences clearly defined. The frequency of loops is reduced in patients of both genders.[20] As regards the quantitative dermatoglyphic features, data have showed an increased total finger ridge count in schizophrenic men and a decreased total finger ridge count in schizophrenic women in comparison with healthy controls of the same gender.[21]

Gabalda and Compton[22] have found no statistically significant differences in dermatoglyphic traits when studying groups of patients with schizophrenia, schizoaffective symptoms and control subjects, nor have they found a correlation between the dermatoglyphic features of the patients and certain clinical symptoms. However, they have reported that there is a connection between certain papillary patterns and the manifestation of specific minor physical anomalies. In this context Gabalda and Compton correlate the increased frequency of ocular abnormalities with the occurrence of loops, especially in patients with schizophrenia compared to patients with schizoaffective symptoms and healthy controls.

The presented data makes it clear that the results from dermatoglyphic studies in schizophrenia are controversial, most likely due to methodological differences, racial and ethnic characteristics of the population studied, as well as the form and course

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of the disease. The differences in ridge patterns between patients and controls assume the presence of biologically operating prenatal factors interacting or non-interacting with the identified genes, which may affect the risk of disease development.[16]

Published data pose the question of sexual dimorphism in the dermatoglyphic features.[23] Males show a significant higher incidence of deviations than females thus supporting the finding that men are more susceptible in their early embryonic development and/or have reduced compensatory mechanisms. This is probably due to gender differences in the development and time of cerebral maturation. Therefore, these results would support the idea that men are more susceptible to dysontogenetic processes in brain development.

PALMAR DERMATOGLYPHICS IN MENTAL DISORDERS

Regarding palmar dermatoglyphic patterns and main palm lines, studies of these traits in psychiatric patients and control subjects are also of great value. The main elements of palmar dermatoglyphics are not different from those of the fingers and thus determine their uniqueness and persistence. Ridge patterns on the interdigital fields, thenar and hypothenar are larger in size, which facilitates the methodology, the study of the details and the identification of quantitative characteristics such as the ridge count and atd angle.

Although there are some inconsistencies in the results of more than 70 published studies on dermatoglyphics in schizophrenia, the a-b ridge count may turn out to be one of the most valuable palmar traits in schizophrenia. The most frequently reported outcomes include reduced a-b ridge count, a higher incidence of radial flexion furrows, ulnar location of the main palm line C and dominant distal axial triradius.[24,25]

A recent meta-analysis of studies published in the period 1983 – 2003 compares the a-b ridge count of schizophrenia patients with that of healthy controls and finds that there are certain contradictions in the results.[26] Our previous studies on palmar dermatoglyphics in schizophrenia suggested that these are tendencies rather than statistically significant differences between the patients and the control group although the total palm ridge count in schizophrenia females and the a-b ridge count in schizophrenia males were found to be decreased.[27] Regardless of these controversies, however, reduced a-b ridge count (sometimes hardly discernible) invariably distinguishes schizophrenia sample from healthy individuals, especially in a subgroup of patients with probably more severe forms of the disease.[26]

These literature data pose the question what defines the a-b ridge count as one of the most essential palmar dermatoglyphic features in schizophrenia. The answer might be found in the prenatal configuration of this palm area. The critical stages in the differentiation of all papillary ridges occur during the third and fourth month of pregnancy. Normal ridge differentiation proceeds in a distal-radial to proximal-ulnar direction. The fetal pads in the II interdigital area (the region of a-b ridge count assessment) are among the first to appear and undergo the longest period of growth and development, while finger ridge patterns are formed later and significantly faster. This defines the a-b ridge count as arguably the most sensitive trait to environmental influences in view of the longest period of prenatal configuration of this area compared to other dermatoglyphic features.[25,28]

FLUCTUATING ASYMMETRY

An important approach in the neurodevelopmental etiology of schizophrenia and bipolar disorder is the assessment of fluctuating asymmetry in dermatoglyphic characteristics. Fluctuating asymmetry was first described by Ludwig (1932) as a sign of ontogenetic stability in different organisms, including humans. It consists of random deviations from perfect symmetry in populations of organisms, a measure of developmental noise, which reflects a population's average state of adaptation and coadaptation during normal morphogenesis.[29] The differences between the right and left homologous structures show a different distribution than normal population, which is approximately zero. Increased asymmetry in homologous structures or highly fluctuating asymmetry shows reduced resistance of the organism to harmful external impacts and has a significant value in the establishment of prenatal operating factors. This is the deviation from perfect bilateral symmetry caused by environmental stresses, developmental instability and genetic problems during development. It is commonly thought that the more symmetrical an organism is, the more able it is to handle developmental stress and the more developmentally stable it is. Fluctuating asymmetry, then, may be a measure of "good-genes" that is difficult or impossible to mask.

Suggestions have been made that polygenetic systems act as a buffer in the development of resistance to adverse environmental influences. The

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replacement of genes in one of these systems can reduce the stability of the body thus increasing the probability of developmental abnormalities and enhancing the fluctuating asymmetry. This fact affects inheritance of anomalies in family history, while certain cases of deviations in the normal development have different etiologies related to the impact of exogenous factors operating during fetal development.[30]

Studies on schizophrenia and bipolar disorder indicate increased fluctuating asymmetry primarily for the a-b ridge count and finger ridge patterns in the patients compared with the healthy controls. The relationship between dermatoglyphic asymmetry and some morphological and functional asymmetry of the limbs and brain hemispheres have also been examined.[31,32] The results do not support the probability of lateralization in schizophrenia or abnormal hemispheric asymmetry in bipolar disorder. It becomes clear that fluctuating asymmetry shows no association with gender or hemispheric dominance manifested by functional asymmetry in the limbs - right- or left handedness.

Fluctuating asymmetry appears to be a biological marker for the indication of time of impact, though it is less informative about the nature of the harmful agent (e.g., edema, or ischemia of the fetus). In terms of dermatoglyphic features, high fluctuating asymmetry is considered a sign of impaired neurodevelopment, which occurs during the formation of papillary ridges (in the months 3 to 5 of embryogenesis). In addition to the a-b ridge count, fluctuating asymmetry in dermatoglyphics may contribute to the establishment of a link between prenatal exogenous events and subsequent structural changes in ectodermal derivatives.

CONCLUSIONS

The multi-aspectual nature of the theories of ridge pattern formation defines dermatoglyphics as a result of complex processes of formation and configuration which occur at the background of an individual genetic determination. The common ectodermal origin, as well as the coincidences in the periods of embryonic morphogenesis of the epidermal patterns and nervous system could explain the vulnerability of ridge patterns and brain structures to exogenous harmful events during the pre- and perinatal period. The existent contradictions in the published data on dermatoglyphics in mental disorders suggest a need for additional studies of these biological markers in order to identify their place in the neurodevelopmental etiological model of these diseases.

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