The European Journal of Psychiatry 36 (2022) 77—93

THE EUROPEAN JOURNAL OF PSYCHIATRY

www.elsevier.es/ejpsy

REVIEW ARTICLE

Biomarkers of mental illness and the human hand: A systematic review

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Received 15 February 2021; accepted 26 January 2022
Available online 24 March 2022

KEYWORDS
Biomarkers;
Mental illness;
Dermatoglyphic;
Palmar crease;
Digit ratio;
Systematic review

Abstract
Background and Objectives: Biomarkers on the hands have been associated with a range of physical and mental health conditions. To systematically evaluate the evidence of dermatoglyphics, digit ratio and palmar crease hand biomarkers in relation to mental illness.
Methods: Web of Science, Scopus and MEDLINE were searched for eligible studies, the review was performed according to PRISMA.
Results: 29 papers comprising of 13,030 participants were selected. Palmar crease research presented the most consistent correlations. Dermatoglyphics presented significant findings, although there were specific biometric inconsistencies in some results. Digit ratio produced the least consistent results, with some non-significant and contrasting results.
Conclusions: The evidence of this review suggests that all three fields, dermatoglyphics, palmar creases and digit ratio, can indicate mental disorders to varying degrees.

Introduction

Mental illness is a collective term referring to diagnosable mental disorders and health conditions involving significant changes in emotion, thinking and/or behaviour, associated with distress and problematic social functioning.[1] However, there are inherent difficulties in defining precise distinctions between normality and psychopathology,[2] and assessment and diagnostic limitations have been widely discussed.[3,4,5,6,7] The DSM provides checklist criteria for assessing mental illness, but the subjective nature of these assessments and their lack of objectivity is a philosophically and scientifically debated issue[8] and as "no definition adequately specifies precise boundaries for the concept of 'mental disorder.'",[9] precisely distinguishing between normal emotional problems and a valid psychological disorder is an enduring issue within psychiatric assessment.[7]

Research into biomarkers for mental illness aims to establish more definitive diagnostic tools for psychological disorders.[10] However, despite decades of research, mental illnesses lack an objective diagnostic assessment and are inhibited by subjective clinical evaluations.[11] Extensive research exploring the neurological, neurochemical, blood-based and genomic biomarkers of psychiatric disorders has been conducted.[12,13,14] However, these areas of research have inherent difficulties and limitations such as distinguishing false positives,[15] identifying

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https://doi.org/10.1016/j.ejpsy.2022.01.007

complex polygenic gene combinations[16] and the cost and expertise required to perform such tests.[10] Therefore, establishing easily examinable, cost-effect, clinical biomarkers for would be beneficial.

The human hand is a uniquely complex appendage from which a vast amount of clinical information can be obtained.[17] The success of the hand in clinical identification purposes stems from the underpinning biological processes that generate its physical characteristics,[18] which explains the utility of their diagnostic assessment in medicine.[19] Many regions of the hand have been studied clinically, but in relation to mental health the dermatoglyphics, digit ratio and palmar creases have been most extensively researched.

The epidermal ridges on palms and fingers, known as the dermatoglyphics,[20] develop from the embryonal ectoderm in the first trimester and have the same morphological origins as the brain, spinal cord and nervous system.[21,22] As well as genetics, dermatoglyphic are influenced by intrauterine environmental disturbances[23] and abnormalities in their patterns have been associated with mental illness including schizophrenia,[24] psychosis,[25] bipolar disorder[26] and autistic spectrum disorders.[27,28]

Palmar creases develop between 7-9 weeks of gestation[29] and are formed through an interplay of genetic and environmental factors.[30] Associations between palmar creases and the central nervous system have been made due to their simultaneous development from the ectoderm[31,32] and genetic abnormalities, teratogens and conditions involving the nervous system have been explored in atypical palmar creases. Such biomarkers have been associated with conditions including schizophrenia,[33] Down's syndrome and developmental problems,[34,35] hyperactivity[36] and intellectual disabilities.[37]

The comparative lengths between the index and ring fingers (2D:4D) is considered a biomarker of prenatal hormonal exposure[38] and is another established biomarker of the hands where a range of mental illnesses have been investigated including depression[38] and schizophrenia[39] and lower ratios with ADHD,[40] eating disorders,[41] and autism.[42]

In order to appraise the value of the hands as a biometric tool, a systematic review is required. The hands represent an external and objective measure that can be assessed with minimal training, diagnostic expertise or costs. This review aims to provide an understanding of the hands' utility as a biometric assessments tool in mental illness, indicate their potential for clinical application and direct future research.

Methods

Search strategy

The search strategy was developed in accordance with guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).[43] Web of Science, Scopus and MEDLINE databases were used to comprehensively search the literature. The fields of 'dermatoglyphics', 'digit ratio' and 'palmar creases' were searched in conjunction with mental illnesses, eg "dermatoglyphics" AND "schizophrenia". Due to the amount of research in each field, data parameters were customized to ensure the latest research was incorporated: dermatoglyphics 2015-2020 and digit ratio 2017-2020. Palmar crease research is comparatively sparse: databases were searched from 1970-2020 to ensure all relevant research was reported.

Study selection

Search results from the databases were extracted to RefWorks and duplicates removed. All titles were read followed by the abstract of relevant articles. Articles that were identified during the title and abstract screening were further assessed for eligibility using pre-selected eligibility criteria and where necessary the full text was reviewed. Articles that were in two groups (eg. dermatoglyphics and palmar creases) were assigned to one based on their primary biometric relevance. Inclusion and exclusion criteria can be seen in Table 1.

Table 1 Selection criteria for articles.

Inclusion criteria	Exclusion criteria
Papers from Peer-reviewed journals, case-control and cross-sectional studies*	Meta-analyses, systematic-reviews, case-studies, articles not published in peer-reviewed journals
Articles in the English language	Articles not in English
Articles within the field specific data-parameters	Articles outside the field specific date parameters
Measures and outcomes were primarily hand-based biometric (dermatoglyphics, digit ratio, palmar creases) assessments of participants with mental illness	Multiple biomarkers were examined and the examination of the hand was not primary (eg minor physical abnormality research).
Mental illness was defined by recognised diagnostic criteria (eg. DSM, ICD) or validated scales (eg. BDI for depression, PANSS for schizophrenia)	Studies examining state or trait personality biomarkers (eg risk-taking, aggression) or studies not examining a recognised disorder according to international diagnostic criteria (eg problematic and pathological internet use, development language disorder)
No restrictions were placed on the participants or populations	Studies examining hand biomarkers not in mental illnesses (eg chromosomal disorders).
	Articles that were inaccessible/non-digitised.

* Case-control studies are primarily used in biometric mental health research and are the most appropriate way to investigate the phenomenon as they have an established diagnosis and clear group distinctions. Biometric mental health research may also incorporate cross-sectional studies, which have been included. Cohort studies are not appropriate for biometric assessment and were excluded.

Quality assessment

Studies meeting the inclusion criteria were assessed for methodological quality using The Effective Public Health Practice Project (EPHPP) quality assessment tool.[44] The instrument provides an established and standardized means to assess quality and bias of the study and provides a rating (strong, moderate or weak) based on: (1) selection bias, (2) study design, (3) confounders, (4) blinding, (5) data collection methods, (6) withdrawals and dropouts, (7) intervention integrity, and (8) analysis.

Data extraction

Data from articles meeting inclusion criteria was extracted. The data extracted included: (a) author, (b) year of publication, (c) country where the study was conducted, (d) sample size, (e) characteristics of cases and control groups, (f) diagnosis, (g) biomarkers examined, (h) biometric measurement used, (i) results, (j) conclusion, (k) limitations, and (l) quality of study (from EPHPP assessment).

Data synthesis

Due to the variety of metrics, assessments and outcome measures it was not appropriate to conduct a meta-analysis. Instead, the relevant recent literature was mapped in a systematic fashion to provide a quantitative descriptive presentation of findings of selected literature in tables. Statistical results reported in the selected study (such as t-test, chi square, odd ratio) were extracted and these results were used to calculate the Cohen d effect size, using the effect size Calculator from the Cochrane Collaboration.[45]

Results

Study selection process

The databases search provided the following results: Dermatoglyphics + mental illness (WoS=135, Scopus = 55, MEDLINE = 5), digit ratio + mental illness (WoS=119, Scopus = 145, MEDLINE = 36), and palmar crease + mental illness (WoS=46, Scopus = 218, MEDLINE = 70); making a total of 829 papers found from the search. Duplicates were removed from each field, leaving totals of dermatoglyphics = 47, digit ratio = 286, palmar crease = 180. Following the screening and selection process, 29 articles (dermatoglyphics = 6 (number of participants= 953), digit ratio 12 (number of participants= 8736), palmar crease 11 (number of participants= 3614 -with total of 13,030 participants) met the criteria and were included in the systematic review (PRISMA flow diagram Fig. 1).

Fourteen studies were excluded at the eligibility stage for several reasons: examining conditions not recognised by the DSM or ICD, such as pathological internet use[46,47]; fetal alcohol exposure[48]; risk of psychosis[49]; development language disorder.[50] Additionally, research where biomarkers in the hand were not the primary assessment tool were excluded.[33,51,52] Studies which did not directly explore the relationship to mental illness and biomarkers and instead looked at mediating factors,[53,54] symptoms,[55] treatment responses,[56] or paternal biometric factors,[57] were excluded. Finally, non-digitised or inaccessible articles were excluded.[58,59]

Study characteristics

Twenty-nine studies that met eligibility criteria were included in the systematic review. Six case-control studies were obtained from the dermatoglyphic search. Oron (2016)[60] research on 'deliberate self-harm' was included as it met the DSM 5 criteria for non-suicidal self-injury disorder and the ICD 10 for intentional self-harm. The digit ratio search produced 12 eligible studies, ten case-control and two cross-sectional. Eleven studies were found in relation to palmar creases, nine case-control and two cross-sectional. Developmental disorder research was included as it met the DSM 5 criteria for attention-deficit/hyperactivity disorder and mild neurocognitive disorder.[61] Total mental illnesses examined can be seen in Table 2.

Generally, studies examined dermatoglyphics, palmar crease and digit ratio selectively. However, some studies incorporated more than one hand biometric subfield eg. palmar creases and dermatoglyphics.[60] Most dermatoglyphic studies examined a range of skin ridge patterning on the palm and fingertips,[24,60,62,63] while others focused on the latter.[27,64] Only Buru, Gozil, Bahcelioglu, Ozkan, & Iseri (2017)[65] incorporated the index, middle and little finger in the digit ratio research; all others exclusively examined the 2D:4D ratio. The majority of palmar crease research focused on the Simian line[66,67,68]; while other studies examined this line and additional crease abnormalities,[69,70,71] secondary creases Cannon et al. (1994)[72] and other specific variations to normality.[73] Domany et al. (2018)[74] and Shamir et al. (2015)[75] research had the most diverse range of hand biometric assessments, examining palmar creases, interphalangeal joints (knuckles), abnormal nail folds, finger flexibility and skin texture.

Results related to trait, state, behaviour or other areas not specifically mental illnesses were not reported. For example, Tegin et al. (2019)[76] study on the digit ratio in relation to bipolar disorder and impulsivity — is not reported here as impulsivity is not a mental illness. Similarly, palmar crease studies that report dermatoglyphic findings outside of the dermatoglyphic specified date parameters (2015-2020) are not reported.

Assessment of risk of bias/quality of selected papers

Quality was assessed using the Effective Public Health Practice Project (EPHPP) quality assessment tool.[44] All selected papers and ratings for each paper were assessed on the criteria set out by Thomas et al. (2004).[44] Levels of bias varied between studies (see Table 3) and specific considerations were made in the assessment. As the majority of studies (n = 25) retrieved case samples from clinical settings in a systemic manner there was a 'somewhat likely chance' of representation of the target population. Studies[77,78] which applied a randomised sampling method with a clinical or other setting achieved a 'strong' rating. Kazemi et al. (2017)[27] used a random sample, but gave insufficient information regarding the process or how the target population was defined, so a 'moderate' score was applied. The EPHPP

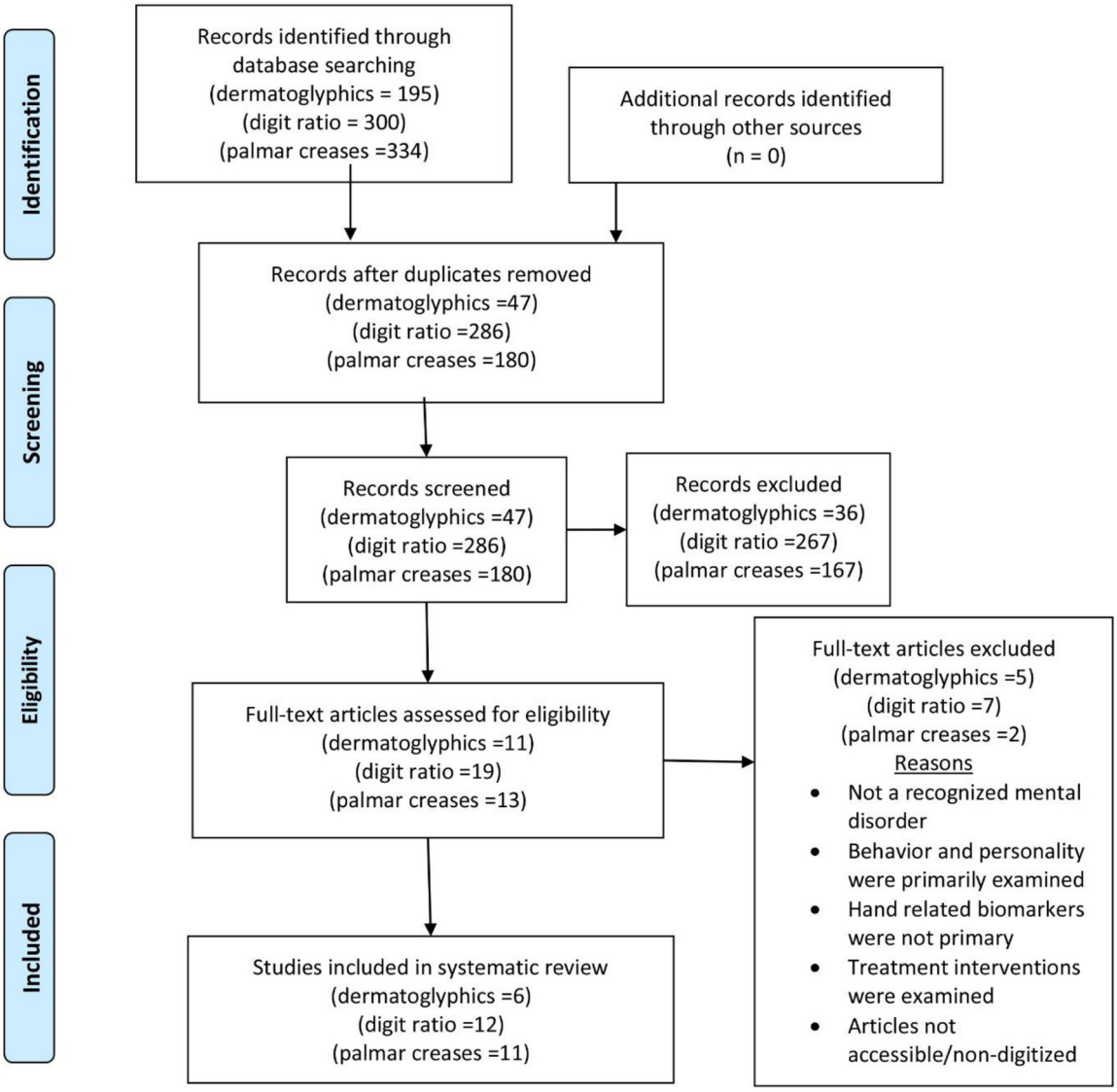

Fig. 1 PRISMA Flow diagram.

Table 2 Mental illnesses examined by the main fields of hand biomarkers.

	Biomarker			
Conditions	Dermatoglyphics	Digit ratio	Palmar Crease	Total
Schizophrenia	2	2	4	**8**
Intellectual disabilities	2	1*	3	**6**
Autism spectrum disorder	1	2*	-	**3**
ADHD	-	4*	-	**4**
Bipolar	-	2	-	**2**
Depression	-	1	1	**2**
Neurodevelopmental disorders**	-	1*	2	**3**
Alcohol dependency	-	1	-	**1**
Gender dysphoria	-	1	-	**1**
Psychosis	-	-	1	**1**
Intentional self-harm	1	-	-	**1**

* Myers et al. (2018) sample provided four categories (ASD, ADHD, ID and NDDs).
** The developmental disorders group is comprised of participants with inhibited function in areas including communication, specific learning disorders, behavioral disorders and minor cerebral dysfunction.

Table 3 EPHPP quality assessment.

	Selection bias	Study design	Confounders	Blinding	Data collection	Analysis	Quality
Dermatoglyphics							
Bandlamudi et al. (2015)[63]	Moderate	Moderate	Strong	n/a	Strong	Weak	Moderate
Kalmady et al. (2015)[24]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Kazemi et al. (2017)[27]	Moderate	Moderate	Moderate	n/a	Strong	Strong	Strong
Sadanandan & Ushadevi (2016)[62]	Moderate	Moderate	Weak	n/a	Strong	Weak	Weak
Oron (2016)[60]	Weak	Moderate	Moderate	Weak	Moderate	Moderate	Weak
Soman et al. (2015)[64]	Moderate	Moderate	Weak	n/a	Strong	Weak	Weak
Digit ratio							
Akgül et al. (2017)[81]	Moderate	Moderate	Moderate	Moderate	Moderate	Strong	Strong
Buru et al. (2017)[65]	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Cansız & İnce (2020)[82]	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Kilic et al. (2019)[83]	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Lenz et al. (2019)[77]	Strong	Moderate	Strong	n/a	Moderate	Strong	Strong
Myers et al. (2018)[78]	Strong	Moderate	Strong	Strong	Strong	Strong	Strong
Sadr et al. (2020)[84]	Moderate	Moderate	Moderate	Strong	Strong	Strong	Strong
Sanwald et al. (2019)[85]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Schieve et al. (2018)[86]	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Strong
Tegin et al. (2019)[76]	Moderate	Moderate	Strong	Strong	Moderate	Strong	Strong
Wang et al. (2017)[79]	Moderate	Weak	n/a	n/a	Strong	Strong	Moderate
Wernicke et al. (2020)[80]	Moderate	Weak	Strong	n/a	Strong	Strong	Moderate
Palmar creases							
Cannon et al. (1994)[72]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Dar & Jaffe (1983)[69]	Moderate	Moderate	Moderate	Weak	Moderate	Strong	Moderate
Demir & Dane (2019)[66]	Weak	Weak	Strong	Weak	Weak	Strong	Weak
Domany et al. (2018)[74]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Eswaraiah (1978)[73]	Moderate	Moderate	Weak	Weak	Strong	Moderate	Weak
Johnson & Opitz (1971)[67]	Moderate	Moderate	Weak	Weak	Moderate	Moderate	Weak
Johnson & Opitz (1973)[70]	Moderate	Weak	Weak	Weak	Moderate	Strong	Weak
Rosa et al. (2001)[37]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Rosa et al. (2002)[71]	Moderate	Moderate	Strong	Strong	Strong	Strong	Strong
Shiono & Azumi (1982)[68]	Moderate	Moderate	Moderate	Weak	Strong	Strong	Moderate
Shamir et al. (2015)[75]	Moderate	Moderate	Moderate	Strong	Moderate	Strong	Strong

scores case-control study designs as 'moderate' applied to most articles in the review (n = 25); the four cross-sectional designs[66,67,79,80] were considered a 'weak' rating according to EPHPP. Eight studies reported blinding methods achieved a 'strong' rating. Studies failing to apply blinding were rated 'weak'. Studies where blinding could have been applied for methodological rigour received a moderate rating; and where blinding was not required due to the quantitative nature of the measure, 'n/a' was reported. The consideration given to case-control confounders varied and studies which reported additional confounders (eg. age, sex, socio-demographic characteristics etc.) were scored as 'strong', whereas studies which only considered the condition (eg. schizophrenia, autism) were scored as 'moderate'. Finally, studies which did not report a clear diagnosis differential between case-controls (n = 4) (eg. controls were selected without mental health assessment) were scored as 'weak'. Data collection was scored in relation to the studies' use of established biometric measurement methods, and analysis was scored depending on the appropriateness of the statistical method/reporting. Overall, the studies had good selection bias, used appropriate data collection and analysis methods and gave sufficient consideration to confounders. Six studies were given an overall 'weak' rating and their results were interpreted with caution.

Synthesis of results

Key characteristics and findings from the 29 articles are presented in Table 4. Cohen's d was calculated for 19 studies, with 10 not providing enough/appropriate data to allow for calculation. Cohen (1988)[87] provided the following guidelines on the interpretation of effect sizes: small — 0.2, medium — 0.5, and large — 0.8. See appendix for depictions of biomarkers.

Study limitations

Additional limitations and threats to validity can be seen in Table 5. The majority of palmar crease studies had limited line classification details which affected internal validity. The same studies generally failed to use blinding which would have somewhat mitigated the effects. Some dermatoglyphic studies performed too many statistical tests with a

Table 4 Summary of study characteristics.

Reference, country and study design	Mental illness, sample size and study overview	Biomarkers	Relevant results	Conclusion	Cohen's d (confidence interval)
Kalmady et al. (2015), India, case-control[24]	Schizophrenia Case (n = 89) and controls (n = 48) Dermatoglyphics assessment in relation to hippocampal volume.	- Total ridge count - Fluctuating (FA) and directional asymmetries (DA) of the a-b, b-c and d-c interdigital dermatoglyphics	DAb-c significantly lower in controls (p = 0.004), and bilaterally correlated with reduced patient hippocampal volume (left: F=5, rpartial=0.32, p = 0.03, right: F=4.7, rpartial=0.31 p = 0.04).	Dermatoglyphic biomarkers correlated with brain structures related to neurological pathogenesis in schizophrenia.	-0.59 (-0.95, -0.24)
Bandlamudi et al. (2015), India, case-control[63]	- Schizophrenia - Cases (n = 100) and controls (n = 100) - Dermatoglyphic comparison	- Total finger ridge count (TFRC) - a-b ridge count - ATD and ADT angle	- The mean TFRC was greater for female cases compared to controls (m=112, m=90.4; X^2 =19; $p < 0.05$;). - a-b ridge count differences between male cases and controls in Group 2 (43, 61; $p < 0.05$). - No case-control ATD angle significance was found	Some dermatoglyphic differences observed, female mean TFRC being significantly greater among cases appears the most relevant finding.	0.97, CI (0.53, 1.4)
Soman et al. (2015), India, case-control[64]	- Intellectual disabilities (ID) - ID children (n = 60) and controls (n = 60) - Dermatoglyphic fingerprint comparison	- Fingerprint pattern (ulnar loop, radial loop, whorls and arches)	- Frequency of arch pattern was lower in ID while controls had comparatively fewer radial loops.	Some biometric differences observed, but there are considerable limitations	-
Sadanandan & Ushadevi (2016), India, case-control[62]	- Intellectual disabilities - ID children (n = 100), controls (n = 120) - Dermatoglyphic comparison	- Fingerprint pattern (ulnar loop, radial loop, whorls and arches) - Total finger ridge count (TFRC), ATD angle and a-b ridge count	- ID males had increased ulnar loops and arches and decreased whorls. - ID females had increased arches and whorls and decreased ulnar loops. - ID children had increased TFRC, ATD angle, and a-b ridge count.	Some biometric differences observed, but there are considerable limitations	-
Kazemi et al. (2017), Iran, case-control[27]	- Autism spectrum disorder - ASD children (n = 88) and controls (n = 86) - Dermatoglyphic comparison	- Ridge counts and fingerprint patterns (whorl, arch, loop) of the right and left thumbs and index fingers.	- Cases index finger ridge count was lower than controls ($p < 0.001$) - Cases right thumb ridge count lower than controls ($p < 0.001$) - Cases had more loops on the left index (p = 0.042) and left thumb (p = 0.04). - Arch prints differed on the left thumb between groups (p = 0.012)	Results demonstrated statistical differences between dermatoglyphics of cases and controls	Left index: 0.99 (0.68, 1.3) Right index: 0.67 (0.36, 0.97) Right thumb: -0.68(-0.98, -0.38)
Oron (2016), Israel, case-control[60]	- Intentional self-harm - Cases (n = 16) and controls (n = 16) - Comprehensive analysis of dermatoglyphics and palmar creases.	- Palmar patterns: a-b and b-c ridge counts, delta C area, proximal transverse crease, Sydney crease, bridged creases, broken creases - Fingerprint pattern (loops, arches, whorls)	- Statically significant case control differences where found in five finger prints patterns ($p < 0.05$) and in seven palmar biomarkers ($p < 0.05$)	Significant differences in fingerprint dermatoglyphics and palmar lines reported.	-
Kilic et al. (2019), Turkey, case-control[83]	- Schizophrenia - Cases (n = 76) and controls (n = 67) - Digit ratio comparison	- 2D:4D ratio	- Female cases had greater right-hand 2D:4D ratios than controls (0.985 vs 0.968; p = 0.005. Male cases were significantly lower than controls (0.951 vs 0.984; $p < 0.001$. - No difference was established in the left-hand ratios between groups	Results indicated the right-hand digit ratio being an indicator of schizophrenia.	Male right-hand: -1.3916 (-1.8734, -0.9098 Female right-hand: 0.7905 (0.265, 1.3159) 0.55 (0.14, 0.95)

Table 4 (*Continued*)

Reference, country and study design	Mental illness, sample size and study overview	Biomarkers	Relevant results	Conclusion	Cohen's d (confidence interval)
Akgül et al. (2017), Turkey, case-control[81]	- Schizophrenia - Case (n = 48) and controls (n = 48) - Digit ratio comparison	- 2D:4D ratio	- Schizophrenics showed significantly increased left-hand 2D:4D ratios (1.0119 ± 0.04 vs 0.9904 ± 0.032; F=7.050 p = 0.009*) - No difference between genders.	Results suggested a higher left-hand ratio is found among schizophrenics, which is not sexually dimorphic.	
Schieve et al. (2018), United States, case-control[86]	- Autism spectrum disorder - Cases (n = 599) and controls (n = 811) - Digit ratio comparison	- 2D:4D ratio	- Female cases had a higher overall mean than controls in both hands and significance was found in the left-hand restricted (no maternal smoking, medication etc.) unadjusted (n = 271, 95.6 vs 94.45, p = 0.049) and adjusted sample (n = 259, 95.28 vs 93.53; p = 0.006).	Female left-hand association is independent of cofounders and, unlike males, is not restricted to specific subgroups.	-
Buru et al. (2017), Turkey, case-control[65]	- ADHD - Cases (n = 104) and controls (n = 346). - Multiple digit ratio comparison	- 2D:4D ratio - 2D:5D ratio - 3D:4D ratio - 3D:5D ratio	- Significant case and control differences found in right (0.96 ± 0.03 vs 0.99 ± 0.04; p = 0.001) and left-hand (1.01 ± 0.04 vs 1.00 ± 0.03; p = 0.004) 2D:4D ratio.	Regarding 2D:4D ratio, ADHD boys had more 'feminine' increased-higher ratios, while ADHD girls had more 'masculinised' lower 2D:4D measurements. Additional biomarkers were found with other digits.	Right hand: -0.79 (-1.1, −0.5) Left hand: 0.31 (0.09, 0.53)
Wang et al. (2017), Taiwan, cross-sectional[79]	- ADHD - Boys (n = 158) Girls (n = 42). - 30% inattentive - 70% hyperactive-impulsive or combined. - 68 had mental illness comorbidities.	- 2D:4D ratio	- Those with disruptive behaviour disorders (DBD) or OCD (n = 37) had lower ratios than children without additional comorbidities (t=2.15, p = 0.033). - In both sexes, ADHD behavioural symptoms and cognitive functioning were not associated with digit ratio.	Findings indicated that digit ratio is not an indicator of ADHD clinical symptoms. However, lower 2D:4D ratios were associated with comorbid disruptive behaviour disorders and OCD.	ADHD and comorbid DBD or OCD: -0.0354 (-0.4, 0.31)
Cansız & Ince (2020), Turkey, case-control[82]	- Bipolar - Cases (n = 74) and controls (n = 74) - Digit ratio comparison	- 2D:4D ratio	- No significant difference found between case and control group in either the right or left hand, nor between males and females.	No biometric findings in relation to mental illness were made	Female RH: -0.5 (-0.96, -0.046) Female LH: -0.31 (-0.76, 0.15) Male RH: 0.3022 (-0.16, 0.77) Male LH: 0.068 (-0.39, 0.53)
Wernicke et al. (2020), Germany, cross-sectional[80]	- ADHD - 192 German (50% male) and 192 Chinese participants (50% male) - Digit ratio comparison	- 2D:4D ratio	- German males: hand ratios negatively correlated with ASRS hyper/impulse (left-hand, r = −0.198, BCa 95% CI=−0.252, 0.137, p = 0.028; right-hand, r = −0.177, BCa 95% CI=−0.369, 0.032, p = 0.044) and right-hand ratio with the ASRS combined scale (r = −0.197, p = 0.044). - Chinese sample: all correlations were negative but none achieved significance. - German females had inconsistent correlations (both positive and negative), neither reaching significance.	Results suggested ADHD is associated with lower 2D:4D ratios, as seen in all groups except German females	German male right-hand: -0.40

Table 4 (*Continued*)

Reference, country and study design	Mental illness, sample size and study overview	Biomarkers	Relevant results	Conclusion	Cohen's d (confidence interval)
Lenz et al. (2019), Switzerland, case-control[77]	- Alcohol dependence - Cases (n = 381) and controls (n = 4608) military recruits - Digit ratio comparison	- 2D:4D ratio	- Digit ratio was significantly lower among cases than controls (0.975 vs 0.981, p = 0.035). - Lower digit ratios associated with: moderate/severe DSM− 5 alcohol use disorder ($p < 0.005$), alcohol related service use (p = 0.046), willingness to purchase higher priced drinks (p = 0.002) and increased anticipation of an alcohol high (total cohort: ρ= −0.033, p = 0.026).	Results strongly indicated an association between lower digit ratio and alcohol dependency and related behaviours.	-
Myers et al. (2018), Sweden, case-control[78]	- ASD, ADHD, ID, neurodevelopmental disorders (NDD) - Twin study- concordant and discordant mono- and dizygotic twins cases (n = 106), controls (n = 132).	- 2D:4D ratio	- An association was found in NDD males digit ratio in the between-pairs model (beta=−0.014, 95% CI −0.025 to −0.002, p = 0.019) and the within-pairs NDD female model (beta= − 0.017, 95% CI−0.035 to 0.000, p = 0.050). - A male association was found in the ADHD between pairs model (beta=−0.015, 95% CI−0.027 to −0.003, p = 0.012) - No relationship was found for ASD (n = 46) or intellectual disability (ID; n = 11).	Male concordant ASD twins had lowest ratio. There was a small association for males between the ratios and any NDD and ADHD diagnoses. Males had lower ratios than females.	-
Sadr et al. (2020), Iran, case-control[84]	- Gender dysphoria - Natal females (n = 104), natal male (n = 86), controls (n = 109) - Digit ratio comparison	- 2D:4D	- Transwomen (natal men) had significantly higher ratios compared to male controls ($F(1, 142) = 4.33$, p = 0.001). - Gender dysphoria (GD) onset (pre- or post-puberty) was associated with lower transmen ratios than late onset (n = 12; $F(1, 102) = 8.55$, p = 0.004).	A lower digit ratio in men and a higher digit ratio in women was associated GD.	Transwomen compared to male controls: 0.3 (0.02, 0.59)
Sanwald et al. (2019), Germany, case-control[85]	- Depression - cases with major depression (n = 139) and controls (n = 137). - Digit ratio comparison	- 2D:4D ratio	- Females had significantly greater BDI-II scores than men (p = 0.006). - No significant association found between BDI-II score and right, left or combined digit ratios. - Sex differences between cases 2D:4D ratio were absent in the right hand, but in controls the 2D:4D ratio was smaller (as expected) in men than women.	Major depression might be associated with the absence of sex differences in the right-hand digit ratio.	-
Tegin et al. (2019), United States[76]	- Bipolar - Bipolar cases (n = 50) and controls (n = 50) - Digit ratio comparison	- 2D:4D digit ratio	- Cases had higher right-hand ratios (0.967± 0.029 vs 0.953±0.035, p = 0.032) - No difference was found in the left hand.	Results suggested bipolar affects the right-hand digit ratio.	0.056 (-0.34, 0.45)
Eswaraiah (1978), India, case-control[73]	- Schizophrenia - Cases (n = 118), controls (n = 536). - Three types of palmar crease formations	- Single radial base crease (SRBC; considered a Simian line variation) - Double radial base crease (DRBC) - Triple radial base crease (TRBC)	- Significant differences found between cases and controls in right ($p < 0.01$) left ($p < 0.01$) and both hands ($p < 0.001$). - Schizophrenics to have had a higher incidence of SRBC and TRBC patterns and lower DRBC patterns.	Palmar crease formations vary among schizophrenics compared to healthy controls	0.5 (0.34, 0.66) 0.502 (0.07, 0.9)

Table 4 (*Continued*)

Reference, country and study design	Mental illness, sample size and study overview	Biomarkers	Relevant results	Conclusion	Cohen's d (confidence interval)
Cannon et al. (1994), Ireland, case-control[72]	- Schizophrenia, cases (n = 43) and age and sex-matched controls (n = 43). - Density of palmar creases examined	- Density of palmar crease and secondary lines	- Seven individuals, all cases, had high density lines (chisquare=5.1, p = 0.02). - Cases were more likely to have: - >5 hospital admissions (chi-square=9.0, p = 0.002) - Higher medication (chi-square=6.2, p = 0.001) - Earlier onset of illness (age<20) (chi-square=3.2, p = 0.07). - No correlation with crease density was found in gender, family history, mental illness or occupation	Increased line density was associated with schizophrenia and disorder severity.	
Shamir et al. (2015), Israel, case-control[75]	- Schizophrenia - Cases (n = 51), mood and anxiety disorders (n = 29), controls (n = 54) - Multiple hand-based biomarkers	- Poorly defined proximal interphalangeal joint - Extended eponychium - Abnormal proximal transverse crease (shortened, fragmented, broken, Simian) - Ill-defined thenar crease - Skin texture - Digital flexibility	- Highly significant biometric differences were found in all biomarkers between cases and controls - Results showed 78.4% identification accuracy between schizophrenics (80.4% sensitivity) and non- schizophrenics (77.1% specificity).	Results strongly suggest utility of hand biometric identification	57.5
Domany et al. (2018), Israel, case-control[74]	- Schizophrenia - Schizophrenics (n = 14) compared to: depression (n = 29), bipolar (n = 14) anxiety disorder (n = 3), OCD (n = 5), PTSD (n = 15) and personality disorder (n = 15). - Multiple hand biomarkers	- Poorly defined proximal - interphalangeal joint - middle digit eponychium - ill-defined thenar crease - abnormal proximal transverse crease (short, broken, fragmented) - finger flexibility	- Discriminate analysis between schizophrenics and non-schizophrenics was highly significant ($p < 0.001$). - Additional analysis between bipolar and PTSD patients was non-significant, indicating specific biometric relevance to schizophrenia - Sensitivity to detect schizophrenics was 78.6%, specificity of non-schizophrenic identification was 80.2%.	Results suggest biomarkers can be used in the identification of schizophrenia over other mental illnesses.	58.8
Dar & Jaffe (1983), Israel, case-control[69]	- Intellectual disabilities - ID children: congenital origin (n = 200), idiopathic (n = 50) and controls (n = 500) - Palmar crease comparison	- Palmar-crease variants (normal, Simian, Simian variation, Sydney line, other abnormality).	- Three palmar creases were found more frequently among cases and control: - Simian line (typical or variant) (7.5% vs 0.2%; $p < 0.01$) - Abnormal/unclassified variants ($p < 0.01$). - Single phalangeal flection crease (as opposed to two) on digit 5 (p = 0.001).	Palmar line pattern differences found between ID cases and control	0.81 (0.66, 0.96)
Rosa et al. (2001), Spain, case-control[37]	- Intellectual disabilities - ID children (n = 62) and controls (n = 75). - Palmar lines	- Hypoplasic (undeveloped) creases - Simian line - Broken creases - Sydney line.	- Cases had lower frequency of normal palmar creases (41.4% vs 71.2%) displaying significantly more hypoplasic (undeveloped) creases, Simian lines, broken creases and Sydney lines ($p < 0.0001$). - Abnormal palmar creases were associated with increased risk of ID ($p < 0.001$, OR = 3,86; 95% CI = 1,77—8,47)	Results support palmar crease biometric variations in ID and suggest developmental disorders have a physiological basis seen in the hands	1.02 (0.65, 1.4)

Table 4 (*Continued*)

Reference, country and study design	Mental illness, sample size and study overview	Biomarkers	Relevant results	Conclusion	Cohen's d (confidence interval)
Shiono & Azumi (1982), Japan, case-control[68]	- Intellectual disabilities Cases (n = 107), controls (n = 694)Palmar crease comparison	- Sydney line - Simian line (complete formation) - Simian line (aberrant formation)	- No significance was found in rates of Sydney line nor complete Simian - Aberrant Simian lines were significantly higher between cases and controls in both males (males, left-hand 27.4% vs 8.8%, right-hand 24.1% vs 9.6%; x^2=15.7040, d.f=1, $p < 0.001$), and females (left-hand 21.2% vs 11.8%, right-hand 26.7% vs 10.3%; x^2=5.3074, d.f=1,0.02< $p < 0.01$)	Results suggested aberrant variations of the Simian line are associated with intellectual disabilities	Males: 1.16 (0.59, 1.7) Females: 0.73 (0.11, 1.35)
Johnson & Opitz (1971), United States, case-control[67]	- Neurodevelopmental disorder - Children with developmental disorders (n = 276) and controls (n = 150) - Examining rates of the Simian palmar crease	- Simian line (single palmar crease).	- Among cases, 11.2% had either a compete (6.5%) or partial (4.7%) Simian, while among controls the biomarker was found in 2%. - Simian lines were associated with lower intellectual ability ($p < 0.05$) and additional physical abnormalities (eg. cleft palate, facial asymmetry, cardiac murmur) (p = 0.02).	Results suggested a relationship between the biomarker and neurodevelopmental disorders	-
Johnson & Opitz (1973), United States, cross-sectional[70]	- Neurodevelopmental disorder - Children (n = 256) from a developmental clinic. - Palmar crease lines	- Simian line, Sydney line and other palmar crease abnormalities	- 65 (25%) children had unusual palmar crease markings (24 Simian, 30 Sydney line). Of those, 37% were mentally disabled (IQ<70) compared to only 17% of children with normal creases. - 50% more congenital anomalies were also apparent in the abnormal palmar crease children - The Simian line was twice as prevalent in those with overt neurologic findings (20% vs 11%)	Abnormal palmar creases were found more frequently than in previously studied normal populations and were somewhat associated with disorder severity	-
Demir & Dane (2019), Nigeria, Cross-sectional[66]	- Depression - 45 men (22 with Simian) and 32 women (16 with Simian) - Simian palmar crease	- Simian line	- Females with a Simian had a significantly increased depression score compared to those without (m=15.15, SD 4.83 vs m=11.06 SD 5.09, p = 0.03). - No association was found in males.	The results suggested a Simian line is associated with depression in females, but there are considerable limitations.	Female cases and controls: 0.8 (0.1, 1.5)
Rosa et al. (2002), England, case-control[71]	- Psychosis disorder - 45 concordant and discordant MZ twins with psychotic disorders and 22 control twins - Abnormal palmar flexion creases (APFC)	- APFC (Simian crease, the Sydney line, very rudimentary creases, and clear broken proximal and distal palmar creases).	- The risk of APFC was 41 percent in affected twins and 19 percent in nonaffected twins (OR = 2.52; 95% CI: 0.74-8.58; one-sided p = 0.10)	The results suggested non-genetic factors contribute to the biometric formations and etiology of psychosis	0.5

Table 5 Limitations of studies.

Study	Limitations
Kalmady et al. (2015)[24]	Relatively small sample Additional dermatoglyphics could have been included, eg. fingerprint pattern, ridge count of ATD angle
Bandlamudi et al. (2015)[63]	- Subdivision of biomarker scores in the groups was unusual and unexplained - Too many statistical analyses performed which could give false significance
Soman et al. (2015)[64]	- Lack of statistical analysis and no p values reported - No sample size calculation - Lack of mental illness definition criteria - No data collection methods reported - No diagnosis of healthy controls
Sadanandan & Ushadevi (2016)[62]	- Lack of statistical analysis and no P values reported - Under-reported information about participants' diagnoses and gender differentiation
Kazemi et al. (2017)[27]	- Unusual and limited assessment of dermatoglyphics; could have included other fingers
Oron (2016)[60]	- Analytical limitations, as it appeared too many tests were run with too small a sample - Too many independent variables allowing significance to be easily found
Kilic et al. (2019)[83]	- The small sample size limited generalisablity - Data collection methods could have been improved with blinding and the use of electronic finger measuring methods
Akgül et al. (2017)[81]	- Small sample size - The study focused equally on the relationship between schizophrenic symptoms and social cognitive abilities, which slightly detracted from its relevance to biomarkers and mental illness
Schieve et al. (2018)[86]	- Children as young as three were included in the study. Asynchronistic bone growth at this age may confound results
Buru et al. (2017)[65]	- The ratios of the middle and little finger had not been previously examined in mental illness and more theoretical justification and discussion is required - Lack of information regarding the control group - Female sample size was small in comparison to males
Wang et al. (2017)[79]	- Lack of control group - Small female sample size
Cansız & Ince (2020)[82]	- Sample was relatively small and may not be generalizable. Blinding measures would reduce risk of bias given the manual caliper used
Wernicke et al. (2020)[80]	- Lack of control group - Both samples were mainly students and results are therefore not representative of the wider population
Lenz et al. (2019)[77]	- Self-reported finger measurements are not as accurate - No direct clinical diagnosis was made - Finger deformity or structural damage was not excluded
Myers et al. (2018)[78]	- Results might not be generalisable to non-twin populations
Sadr et al. (2020)[84]	- The pre- and post-puberty onset transmen (natal female) group had a very small sample size (post-puberty n = 12) and the results should be considered preliminary
Sanwald et al. (2019)[85]	- Depression severity as a changing state variable and as digit ratio is a fixed biomarker. The association between depression and digit ratio could be limited - Trait depression measures could have been applied to align the trait biometric assessment - Cases were being treated with medication which could have affected symptom severity and BDI scores
Tegin et al. (2019)[76]	- Limited sample size inhibited generalizability - Only three cases were diagnosed with bipolar 2, restricting results primarily to bipolar 1
Eswaraiah (1978)[73]	- Limited line classification system with poorly defined boundaries - Significance of individual crease patterns not reported - High likelihood of bias given subjective nature of the assessment, lack of blinding and multiple judges
Cannon et al. (1994)[72]	- Follow-up study required; line density not widely studied - Relatively small sample - Lack of theoretical discussion and potential causes
Shamir et al. (2015)[75]	- Anxiety and mood disorder group could have had confounding mental illnesses affecting results - Relatively small sample size

Table 5 (*Continued*)

Study	Limitations
Domany et al. (2018)[74]	- Non-schizophrenic patients may have had confounding disorders as they were selected based on their primary diagnosis - Small sample of schizophrenics
Dar & Jaffe (1983)[69]	Definition of abnormal palmar creases not well established Only one example picture given and was unclear Multiple judges conferring would be more rigorous and reduce bias Very small percentage of control Simian lines (0.2%) may suggest a measurement error as previous reports for Israelis are close to 5%
Rosa et al. (2001)[37]	- Limited female sample (n = 19) size
Shiono & Azumi (1982)[68]	- Diagnostic criteria in both groups not clearly defined - Assessors of biomarkers should have been blinded to reduce bias - Inherent subjectivity defining types of Simian and Sydney lines
Johnson & Opitz (1971)[67]	- Categorising the Simian is subjective and validity could be inhibited - Blind judges would have reduced bias - Diagnosis and inclusion criteria for mental disorder was vague
Johnson & Opitz (1973)[7]	- Lack of control group - Poor diagnostic recruitment. Although children were referred to the clinic, developmental disorders may not have been established and additional specific examination could have been conducted.
Demir & Dane (2019)[66]	- No reporting on data collection - No classification method of Simian line was specified — greatly weakening validity - No explanation of sampling, inclusion or exclusion criteria
Rosa et al. (2002)[71]	- Small sample size and rates of APFC, resulted in wide CI - Larger sample required to establish findings

high number of independent variables, which appeared to produce significant findings through excessive testing. Sadanandan and Ushadevi (2016)[62] and Soman et al. (2015)[64] studies had serious limitations, did not apply statistical analysis and only reported observational findings. Among all research categories there were incidents of small sample size which undermined both internal and external validity and often, in such studies, replication was warranted. Additionally, the date parameters for dermatoglyphics and digit ratio were capped to incorporate only the latest research in the field, therefore prior and potentially significant research in each area could have been excluded.

Summary of results

All studies except some research[79,82,85] reported biometric indicators of mental illness. Palmar crease research presented the most consistent findings and while there were some inconsistencies in dermatoglyphics, there was clear biometric correlations to mental illness. Digit ratio also showed associations with mental disorders, but had inconsistencies and contradictions among the research.

Discussion

The aim of this study was to systematically evaluate the evidence of dermatoglyphics, digit ratio and palmar crease hand biomarkers in relation to mental illness. Three primary fields of hand biomarkers were systematically examined for their biometric relationship to mental illness: dermatoglyphics, digit ratio and palmar creases. Of the 29 studies reviewed, effect sizes were calculated for 19, with 10 providing insufficient statistical information for the calculation of Cohen d. All reported significant findings, except three digit ratio studies.[79,82,85] Two[62,64] did not report p values therefore significance could not be ascertained. Palmar crease research demonstrated constancy across all papers, with all findings corresponding. Dermatoglyphics presented some inconsistencies: Bandlamudi et al. (2015)[63] and Kalmady et al. (2015)[24] had slightly different reports on specific schizophrenic biomarkers, as did Soman et al. (2015)[64] and Sadanandan and Ushadevi (2016)[62] among intellectual disables. Digit ratio produced more inconsistences than the other groups, with non-significant findings and some contrasting results presented in schizophrenia between Kilic et al. (2019)[83] and Akgül et al. (2017)[81]; ADHD between Wernicke et al. (2020),[80] Myers et al. (2018),[78] Buru et al. (2017)[65] and Wang et al. (2017)[79]; and ASD between Schieve et al. (2018)[86] and Myers et al. (2018).[78]

Of the 12 mental illnesses in this review, only bipolar, examined by two digit ratio studies,[76,82] did not appear to be indicated by biomarkers. Evidence for biometric indications in schizophrenia was strong, with significant results produced in dermatoglyphics,[24,63] palmar creases,[72,73,74,75] and digit ratio.[81,83] Intellectual disables were strongly indicated, particularly in palmar crease research,[37,68,69] and some indications in the dermatoglyphic studies.[62,64] Neurodevelopmental disorders were associated with both palmar crease[67,70] and digit ratio.[78] Individual studies also examined intentional self-harm,[60] alcohol dependency,[77] gender

dysphoria[84] and psychosis,[71] with each showing significant biometric correlations. Autism spectrum disorder, ADHD and depression produced slightly inconsistent results and, as with bipolar, require additional studies incorporating more biometric categories to be conclusive.

Dermatoglyphic evidence

Dermatoglyphic studies showed a reasonably consistent relationship to mental illness. The studies reviewed used a wide variety of variables, with no study using the exact same biometric assessment of dermatoglyphics. As a quantitative measure minimal bias could occur, and all six studies adhered to standardized contemporary classifications.[88] Effect size was calculated for half of the studies, with Soman et al. (2015),[64] Sadanandan and Ushadevi (2016)[62] and Oron (2016)[60] providing insufficient statistical information to do so and thereby limiting the known magnitude of the research. The three studies[24,27,63] for which Cohen's d was calculated all showed medium to large effect sizes, ranging from -0.59 to 0.99 (see Table 4).[89]

Four of the six studies were conducted in India, which probably represents a current cultural interest in this field; historically seminal publications were from North America, Europe and East Asia.[90,91] As dermatoglyphics vary between ethnicities,[92] the results in the present review may not be generalizable to western populations and further research may be required to validate the findings cross-culturally. Overall, the evidence from this review supports the association of dermatoglyphics and psychological conditions and suggests specific skin ridge patterns could correlate with mental disorders and represent affected neurodevelopment. There is a range of dermatoglyphic variables available (for example fingerprint patterns, finger and palmar ridge counts and atd angle) for examination and, although individually the assessment of dermatoglyphics was generally appropriate for each study, future research should aim to develop specifically on previous findings and base assessments on precise dermatoglyphic biomarkers to help build, establish and advance the literature concisely and systematically. This would help establish specific dermatoglyphic variants relating to specific psychological conditions which would advance practical biometric applications.

Palmar crease evidence

All palmar crease studies reported significant and consistent findings. Eleven papers were reviewed, with two[67,70] not providing the appropriate statistics for effect size calculation. For the nine studies that did, Cohen's d ranged between medium and large 0.5-1.3 (see Table 4). Compared to digit ratio and dermatoglyphics, palmar crease research involves a higher risk of bias due to the qualitative nature of line classification systems. Improved methods of classifying the palmar creases have been devised,[93] but early studies in this review were based on limited evaluation methods. With this inherent subjectivity, there was a necessity for blinding which only five studies applied, reducing internal validity in the remaining six. Overall, palmar crease studies were highly consistent with corresponding studies and previous literature. However, the methodological limitations were more prevalent and generally there was a higher risk of bias primarily due to the rudimentary line classification system standardized in earlier research. Replicating studies based on improved line classifications is recommended. Compared to digit ratio and dermatoglyphic research, there is a paucity of palmar crease research relating to mental health and to incorporate sufficient and relevant research, studies from 1970 onwards were reviewed. Considering the highly consistent results of the studies available further research in the field is justified.

Digit ratio evidence

Twelve 2D:4D ratio papers were reviewed; all had minimal bias and good methodological procedures. Cohen's d was calculated for eight studies and ranged between low 0.056 and very large -1.3916 effect size (see Table 4). Two studies did not provide sufficient statistical information for the calculation[77,86]; one did not produce significant results[85]; and another[78] produced results too complex to extract into a single effect size (concordant and discordant mono- and dizygotic twins, separated by gender and multiple mental illnesses, were all examined). Similar to the dermatoglyphics research, there was a predominance of in studies from one country (Turkey; $n = 4$), which may reflect recent interest. All studies except one[85] produced significant findings; however there was less consistency than with dermatoglyphics and palmar creases, and the results did not always support previous research.

Digit ratio research is based on the model of prenatal testosterone and estrogen affecting brain circuitry and the resulting symptoms and behaviours associated with certain disorders. Hormones appear to influence disorders such as ADHD and depression,[94] but this systematic review provided mixed evidence for the 2D:4D ratio as a biomarker. A possible reason could relate to the underpinning theory of digit ratio as a proxy for prenatal hormonal exposure. As a surrogate measure of these hormones, the digit ratio is expected to correlate with disorders associated with hormonal influences. However post-natal hormones, as opposed to prenatal, may also influence mental disorders such as ADHD or depression,[80] which could explain variations in the findings.

Another possibility is that due to the multifactorial components of mental illness, pre-natal androgen exposure may not be a powerful enough predictor of a psychological disorder. Additionally, as a single biomarker that is naturally variant in normal populations,[95] the digit ratio is unlikely to account for more than a small percentage of the variation in mental illness. Confounding variables may also impact the results. Environmental and genetic factors affect the digit ratio[96] and studies have specifically shown personality traits,[97,98,99] race and ethnicity,[100] pre-natal teratogen exposure[101,102] and medical conditions[103] all influence relative 2D:4D lengths. In this review, only Schieve et al. (2018)[86] accounted for multiple in-depth confounders, which the results validated as several findings changed when adjusting for these factors. Therefore, such confounders could influence other results and generate inconsistencies. Overall, it appears the digit ratio could be an indicator of certain mental illnesses such as ADHD, ASD or alcohol dependency, but additional systematic reviews on specific disorders would give a more complete understanding.

This study had limitations to consider. Given the heterogeneity of the studies the results may not be generalizable or representative of all populations as palmar creases, dermatoglyphics and digit ratio have all been shown to vary according to ethnicity.[92,100,104] Due to the varying amount of research in each biometric field, the same date deadline could not be used for all and some palmar crease studies were considerably older than others. Additionally, the narrower date deadlines for dermatoglyphics (2015-2020) and digit ratio (2017-2020) meant that relevant findings not within the parameter were not included. The quality of the selected studies varied, with all digit ratio studies being 'moderate' or 'strong'; whereas dermatoglyphics had three 'weak' methodological assessment ratings,[60,62,64] and palmar crease had four 'weak' studies.[66,67,70,73] Due to inconsistent statistical reporting and widely varying methodological quality, a meta-analysis was not able to be conducted. Only papers in English were selected, excluding possibly relevant foreign findings. Publication bias could have occurred, as non-published research that may have produced relevant findings was not accessible. By assessing biomarkers in the whole hand, an informative overall evaluation was constructed. In relation to dermatoglyphics and digit ratio, where there is a significantly greater body of literature, individual systematic reviews may be required to draw conclusive evidence as to their biometric efficacy in mental health. As an exploration of mental health conditions, this review provides a comprehensive general evaluation of the subject in relation to hand biomarkers; but the results are not condition specific. To sufficiently evaluate the efficacy of hand biomarkers in a specific disorder (eg. schizophrenia) a review is required.

Conclusions

The evidence of this review suggests that all three fields, dermatoglyphics, palmar creases and digit ratio, can indicate mental disorders to varying degrees. Palmar crease research most consistently showed a correlation to mental illness although did incur higher risks of bias than the other fields. Dermatoglyphics was the next most consistent, with studies generally finding similar significant results with some inconsistencies. Digit ratio was the least consistent and, as a single biometric assessment, was perhaps too limited to account for the complexity of psychological disorders to a degree of high magnitude. This review indicates that biomarkers in the hands can indicate mental illness.

Future perspectives

Psycho-diagnostic biomarkers are increasingly sought, to assist in mental health assessment, predict onset, evaluate treatment response and instigate interventions.[105] This study provides preliminary evidence to suggest easily identifiable and cost-effective biometric assessment for mental illness could perhaps be developed. With further research and refinement of precise biomarkers in relation to specific mental illnesses, hand biomarkers might have the potential to be integrated alongside other mental health screening tools and assessments and, through the identification of specific markings in the dermatoglyphics, digit ratio and palmar creases, aid in the diagnosis of mental illness. Although, in order to establish the clinical efficacy of hand biomarkers further research considerations are advised. Shamir et al. (2015)[75] and Domany et al. (2018)[74] studies comprised multiple biomarkers in the hands in schizophrenic assessment and yielded identification accuracy of approximately 80%; demonstrating the potential for a clinical diagnostic aid. A large number of studies[24,27,69,73] incorporated multiple biometric assessments within their subfield (eg. multiple dermatoglyphics, multiple palmar creases) which the results of this review show are generally superior to a one-dimensional assessment (eg. digit ratio) in terms of predictive power and magnitude. Therefore, in order to obtain the necessary predictive power and >80% sensitivity and specificity required for clinical use,[106] combining correlated biomarkers in dermatoglyphics, palmar creases and digit ratio is recommended. Future studies should incorporate the findings from this review that show: 1) multiple dimensions of the hand have components that correspond to mental illness; and, 2) combining relevant biomarkers in a diagnostic assessment would yield more powerful results. Establishment of such hand biometric assessments could be used in assessing and in identifying individuals at risk of mental illness. Ethical considerations must be considered. In developing diagnostic biomarkers, there is a risk that important communication between practitioner and client could be undermined by diagnostic expedience.[105] Discrimination could arise with individuals being judged on biomarkers, irrespective of their symptomology. Additionally, employers, insurance companies, family members and friends developing bias and judgements is an important consideration. Further work is required to understand the ethical implications of hand biomarkers in clinical diagnosis.

Ethical considerations

The secondary data was collected from databases following clear systemic review guidelines. No personal information was collected and all data was stored electronically in accordance with the University's data protection policy. All research was conducted in accordance with University of Liverpool's Research Ethics Committee

Declaration of competing interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix. Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.ejpsy.2022.01.007.

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