

*Review***Morphological integration in human skull and its possible role in etiogenesis of neuropsychiatric disorders: Deciphering the link between evolution, development and disease**Ashutosh Kumar^{*1, 5}, Sada Nand Pandey^{2,5}, Muneeb A. Faiq^{3,5}, Vikas Pareek^{4,5}, Ravi K. Narayan^{1,5}

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Abstract

Structure - function interdependence is a universal phenomenon in biological systems. Any alteration in structural features may result in change in functions—leading to natural selection of a particular trait, or dysfunctions thereof. Many such alterations arise during the course of evolution of a species and may meticulously be traced during embryonic development of an organism. Through the theoretical construct of morphological integration, a set of phenotypic traits alter in a coordinated and integrated manner during evolution and embryonic development of an organism yielding efficient environmentally adapted physiological functions pertinent to those structures. Such integration may go awry sometimes, setting the basis for genesis of diseases.

Morphological integration in human skull has been established through various methods. The brain-skull co-development is handcuffed through evolution and development, and the very basis of a neuro-psychiatric disorder could be underlying in dysmorphogenesis of the skull, its consequent effect on structures, and thus functions of the pertinent brain components. Here we propose that morphological integration in human skull may be mechanistically implied in etiogenesis of certain neuro-psychiatric disorders and should be borne in mind during clinical diagnosis and therapeutic interventions.

Key words: Morphological integration; dysmorphogenesis; skull; etiogenesis; neuro-psychiatric disorders

1. Introduction

Morphological integration implies simultaneous alterations in a set of phenotypic traits of an organism in the course of evolution, and embryonic development, to acquire the most efficient and environmentally adapted physiological functions pertaining to those structures [1]. (In morphological integration a set of phenotypic traits vary in common. Modularity bears a conceptual similitude, where simultaneously varying traits are compartmentalized as modules— showing stronger intra-modular than inter-modular co-variance [2].) Morphological integration in human skull has evoked curiosity of the neuropsychiatry investigators for long. It has now been established through various scientific methods [3–6], and its molecular and genetic basis [3,7] has also been established.

Morphological integration provides rationale to explore the very basis of few neuro-psychiatric disorders, whose etiogenesis remains still elusive. A structural basis has, however, been speculated; as in the case of epilepsy [8,9], schizophrenia [10,11], bipolar disorder [12], and certain types of migraines [8,9]. This also presents a missing link connecting evolution, embryonic development and multi-factorial etiogenesis of such disorders. Evidences

have been documented for the ontogenetic integration of skull landmark variations in modern and archaic humans [13,14]. An ontogenetic-evolutionarily linking integration of phenotypic variations across generations in hominid skulls has also been marked in literature [13,15]. The narratives derived from available studies suggest that accumulating effects of erroneous cranio-cerebral development, which have been registered in the genomic structure of a population following the evolutionary trail, may emerge as a neuropsychiatric disorder [3,16–18].

2. Evolutionary aspect

The three dimensional architecture of the human skull passes through continuous and well-orchestrated re-modeling in response to evolutionary changes in its each part [4,19]. Even a small change in the dimensionality of a single landmark, in the course of evolution, has capacity to redirect the dimensionality of all the skull landmarks, and hence to create a different data set of measurements for inter-landmark distances [3]. Although, such a re-modeling of the human skull may not always result in a functional gain and may predispose individuals to certain neuro-psychiatric disorders [8,20,21], as a cost to the evolutionary benefits of the survival [22–24].

The human skull shows tremendous inter-individual variations [25,26] in its anatomy and dimensionality of the landmarks, which may be pronounced in a population representing admixture of different ethnic groups [27], as for example, Indian [28–31] and American populations [32]. Plausibly, these variations accumulated in the long course of evolution (33–35), through assimilation of co-variances [34,35] and epigenetic changes [36] in the gross and genetic structure of a population respectively, implied morphological integration [34,37]. The inclusion of variations in the skull components in the course of evolution might have subjected a population to acquire and propagate multiple errors at the molecular level [3] and to express these as aberrant genotypes and phenotypes [38], setting basis for etiogenesis of certain neuro-psychiatric disorders [7,10,12,18].

3. Developmental aspect

Morphological integration may be instrumental in the developmental causality of the neuropsychiatric diseases (a physiological form of developmental integration at multi-levels and across multiple structures is often called ‘developmental modularity’). An erroneous developmental process can introduce disease at multiple structural levels, and in multiple organs, due to inter-relationship and connectedness of a developmental process [39].

Studies of morphological integration in the skulls of birds [6] and animals [40] including humans [3,41,42] suggest that individual components of the skull maintain tight interdependence with each other in terms of dimensionality, and a change in the dimensions of the any component may also be reflected in other cranial components [3]. This concept may be better understood by observing the interdependence of dimensionality in a deformed human skull where dimensional changes in any of the components would be reflected in whole of the skull. Now as the skull contains brain in closed and filling proximity, certainly a deformed skull has to harbor a correspondingly deformed brain. The development of skull and brain go in tandem [16] and a cranial deformity may present as a craniofacial anomaly, the associated dysmorphogenesis of brain may result in compromised neural functions at birth or may manifest as a neuro-psychiatric disorder later in life [8,10,12] depending upon the degree of disruption and consequent remodeling of molecular regulation in developing brain [21,39].

4. Genetic aspect

The evolutionary and developmental influence on the expression of phenotypic traits can be traced in the genomic structure of an organism. Integration of various phenotypic traits during the course of evolution, may be an outcome of selection pressure, but it gets strictly registered in genetic structure of the organism [43]. In a population, the genomic assimilation of the naturally selected genotypic variants, or sequence reading errors; or fresh mutations, may leave its impact on functions of complete genome, thus, influencing further phenotypic expressions [3,43]. Genetic integration has been confirmed in the human skulls [3], and the evidences indicate that a particular skull dysmorphogenesis may be a phenotypic expression of such a faulty genetic integration [3,16] which may manifest as neuro-cognitive dysfunction [17,18].

5. Functional modularity: Integration of function

‘Functional modularity’ is a functional equivalent to morphological integration and often used interchangeably. Functional modules [1,15] are the sets of related functions which are coordinated together in a biological system [39,44].

6. Literary evidences linking etiogenesis of neuro-psychiatric disorders

Morphological integration enjoys good support from various studies in literature which associate developmental dysmorphogenesis of skull (and consequently of brain) with genesis of certain neuro-psychiatric disorders, which include various craniofacial anomalies (ending in neuro-cognitive dysfunction) [8], syndromes featuring mental retardation [7,21], and distinct psychiatric diseases [17,18]. Associated studies assert that it may be one of the etiomechanisms involved in causation of such diseases [8,17,18]. A study established links between posterior cranial fossa dysmorphogenesis and major depression [20]. Studies also linked skull dysmorphogenesis with schizophrenia [10,11,17], bipolar illness [12] and other psychoses [18]. It has also been linked to non-psychotic neurological problems like epilepsy [8,9], and migraines [8,9].

7. Conclusions

Association of various neuro-psychiatric diseases to evolution and embryonic development of skull and brain can be speculated through morphological integration, which provides a conceptual basis for understanding links between evolution, development and disease etiogenesis.

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