An abundance of developmental anomalies and abnormalities in Pleistocene people

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Diverse developmental abnormalities and anomalous features are evident in the Pleistocene *Homo* fossil record, varying from minor but rare dental, vertebral, and carpal variants to exceptional systemic disorders. There are currently 75 documented anomalies or abnormalities from 66 individuals, spanning the Pleistocene but primarily from the Late Pleistocene Middle and Upper Paleolithic with their more complete skeletal remains. The expected probabilities of finding these variants or developmental disorders vary from <5% to <0.0001%, based on either recent human incidences or relevant Pleistocene sample distributions. Given the modest sample sizes available for the skeletal or dental elements in question, especially if the samples are appropriately limited in time and geography, the cumulative multiplicative probability of finding these developmental changes is vanishingly small. These data raise questions regarding social survival abilities, differing mortuary treatments of the biologically unusual, the role of ubiquitous stress among these Pleistocene foragers, and their levels of consanguinity. No single factor sufficiently accounts for the elevated level of these developmental variants or the low probability of finding them in the available paleontological record.

paleopathology | Paleolithic | dysplasia | crania | dentition

Morphological and paleopathological assessments of Pleistocene human remains have identified a variety of skeletal and dental configurations that are either clearly pathological and/or lie substantially outside of the expected ranges of variation for the human group in question (1, 2). Some of these changes are reflections of growth arrest periods during development, others are related to common degenerative processes with age and activity levels, and still others are due to minor or major traumatic insults. However, a substantial number of these abnormalities reflect abnormal or anomalous developmental processes, whether as a result of genetic variants altering developmental processes or as the products of environmental or behavioral stress patterns altering expected developmental patterns.

The recorded cases of systemic developmental abnormalities include hypophosphatemia, hydrocephalus, acromesomelic dwarfism, and systemic dysplasias (*SI Appendix*). The craniocervical changes include premature and delayed sutural synostosis, maxillary alignment, torticollis, foramina parietalia permagma, and condylus tertius. The dental changes involve agenesis, polygenesis, gemination, fusion, dens evaginatus, amelogenesis imperfecta, and distal molar megadontia. Deficiencies of synchondrosis fusion are found in the vertebral columns and the carpal remains, along with appendicular metaphyseal nonfusions. Unusual dimensions and proportions relative to the appropriate human groups are also present. These abnormalities are joined by a number of cases of unknown proximate as well as ultimate etiologies.

Some of these developmental abnormalities are unusual but not exceptional in recent human samples, and thus it would not be surprising to find examples of them in the (albeit limited) human paleontological record. However, other abnormalities are extremely rare in recent human populations, and the probability of finding such a case in the fossil record would be extraordinary, especially if the relevant sample were considered the approximately contemporary (in geological terms) and neighboring (in continental terms) known specimens. In addition, there is a series of specimens for which concerted efforts have failed to find a recent human parallel or etiology.

For these reasons, the currently documented developmental abnormalities of Pleistocene *Homo* have been brought together, individually summarized (*SI Appendix*), and their implications discussed. From a paleopathological perspective, as well as a paleoanthropological one, the level and pattern of these unusual human remains raise questions about the survival, stress levels, population dynamics, and mortuary behavior of Pleistocene people.

Results

The Pleistocene *Homo* fossil record includes specimens ranging from isolated bones or teeth to largely complete skeletons, with 75 developmental abnormalities deriving from 66 individuals (Fig. 1; descriptions and discussions of each case are provided in *SI Appendix*). The pooled age distribution of the ageable specimens (2 infants, 6 children, 4 juveniles, 6 adolescents, 30 prime age adults, and 8 older adults) differs only modestly from the pooled distribution for Middle Pleistocene through Early/Mid Upper Paleolithic ages at death ($P = 0.146$) (*SI Appendix*, Table S1).

The developmental anomalies vary from minor ossification variations, such as the os centrale partial fusion of the Krapina, Shanidar, and El Sidrón scaphoid bones and the Atapuerca-SH

Significance

The patterns and incidences of developmental abnormalities and anomalies through Pleistocene human evolution may provide insights into issues of survival, stress, consanguinity, and mortuary behavior among these foraging populations. A synthesis of these developmental variants through the *Homo* fossil record provides 75 cases from 66 individuals, an exceptional total given the small paleontological samples. These are primarily from the past 200,000 years, given better preservation through burial, but are known from up to 1.5 million years ago. One-third of them have moderately low probabilities ($P < 0.05$), yet 14% are very rare ($P < 0.0001$), and 19% have no known etiology. No single factor accounts for the extremely low cumulative probability of finding these abnormalities, but this raises questions concerning the natures of Pleistocene human populations.

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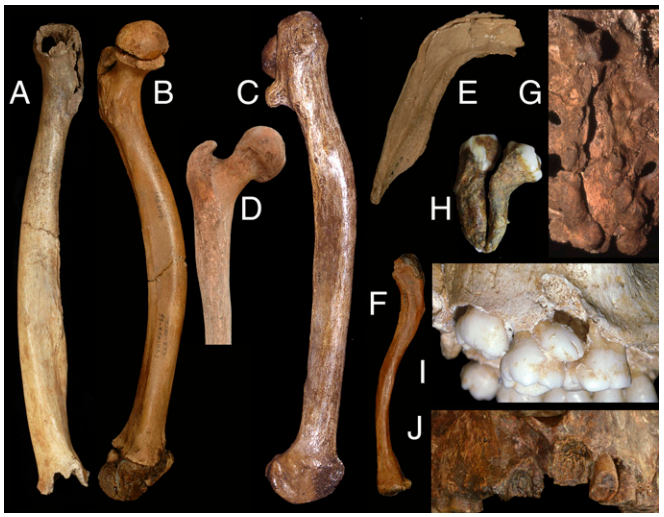

Fig. 1. Examples of developmental abnormalities among Pleistocene humans. (*A*) Tianyuan 1 femoral distal diaphyseal crest. (*B*) Sunghir 3 femoral abbreviation and curvature. (*C*) Dolní Věstonice 15 femoral abbreviation and curvature. (*D*) Arene Candide 2 lesser trochanter absence. (*E*) Palomas 23 mandibular flange. (*F*) Sunghir 1 clavicular elongation. (*G*) Shanidar 1 elongate sacral hiatus. (*H*) Lazaret 18/19 fused premolars with dens evaginatus. (*I*) Pataud 1 double paramolars. (*J*) Dolní Věstonice 16 palatal misalignment. (Not to scale.)

and Villabruna L5 spondylolysis, to serious systemic disorders, such as the hydrocephaly of Qafzeh 12 and the acromesomelic dwarfism of Romito 2 (*SI Appendix*). A number of them would have been inconsequential to the individuals involved, such as the Kebara 2 and Shanidar 3 L1 ribs or the body proportions of Cussac L2A, whereas others, such as the amelogenesis imperfecta of Garba IV-E43, the hydrocephaly of Qafzeh 12, and the hypophosphatemia of Arene Candide 3, would have had serious physiological effects which in the first two cases were likely responsible for early death. All of these individuals (except the Krems-Wachtberg neonates) survived their developmental disorders to some extent, and a number of them persisted with levels of activity similar to those of unaffected Pleistocene people; this persistence is especially evident in the limb bones of Arene Candide 3, Dolní Věstonice 15, Regourdou 1, and Sunghir 3 (3–6).

The cases of developmental abnormalities span the Pleistocene *Homo* record, from the Early Pleistocene Nariokotome, and Garba IV fossils to the terminal Pleistocene Arene Candide, Rochereil, Taforalt, and Villabruna remains. The sample is nonetheless biased toward the Late Pleistocene Middle and Upper Paleolithic with its more complete skeletal remains, many from burials (Fig. 2). The Late Pleistocene sample is also biased toward western Eurasia and northern Africa, due to both fossil preservation and the concentration of paleopathological analyses in that region.

The abnormalities can be divided into those that should occur in <5%, <1%, <0.1%, and <0.01% of individuals, based on either their incidences in recent human samples or the positions of the specimen relative to relevant Pleistocene morphometric distributions (Fig. 3, Table 1, and *SI Appendix*). To these abnormalities are added 13 cases of unknown etiology. (Four cases of known etiology but without incidence data are not included in the distributions.) One-third (33.8%) of the sample providing probabilities (n = 71) are moderately common, expected in 1–5% of cases. However, 26.8% of the abnormalities are rare (<0.1%), and 14.1% are very rare (<0.01%), sometimes extremely so (e.g., <0.0001% for Romito 2, ∼0.001% for Atapuerca-SH Cr.14, ∼0.004% for Xujiayao 11, and ∼0.005% for Arene Candide 3). In addition, for 18.3% of the cases, it has not been possible to determine the etiology of the obvious abnormalities; some of these cases (e.g., Dolní Věstonice 15) represent general appendicular dysplasia but of a undiagnosable form despite his largely complete skeleton, whereas other abnormalities (e.g., the Palomas 6 and 23 mandibular flanges, the Sunghir 3 femora, the Tianyuan 1 femoral crests) are unknown in recent human remains and thus of unknown etiology. Therefore, one-third of the sample has either a markedly low expected incidence or no current diagnosis.

A minority of the unusual aspects occur in multiple individuals from the same level of a site, and hence individuals who may well have been closely related (e.g., the Palomas 6 and 23 mandibles, the Shanidar 4, 6, and 8 or the four El Sidrón scaphoids, the Oase 1 and 2 distal molars). If each of those sets of specimens is counted as one, the percentage of cases with incidences of <0.01% becomes 15.9%, and those of unknown etiology rises slightly to 19.0% (n = 63) (Fig. 3). The same adjustment to the distribution by time period modestly reduces the relative abundance of Middle and Upper Paleolithic cases (Fig. 2).

Some of the incidence/probability levels for individual specimens could be adjusted modestly, given variations or ambiguities in their frequencies among recent humans and/or the appropriateness of the reference samples (*SI Appendix*). It is also unclear the extent to which modern human clinical data are directly relevant to the assessment of incidences in the Pleistocene. However, minor adjustments to the levels would have little effect on the basic pattern, that there is both a high level of anomalies/abnormalities among these Pleistocene humans and a substantial portion of them should have been extremely rare.

Consequently, although some of these Pleistocene *Homo* specimens have moderately common developmental deviations, a substantial number of them would be exceptional to find in a recent human skeletal sample. Given the limited size of the human fossil record and of associated skeletons, there are surprising numbers of developmental disorders or anomalies before the Upper Paleolithic and especially before the Late Pleistocene. In most individual cases, the number of relevant comparative

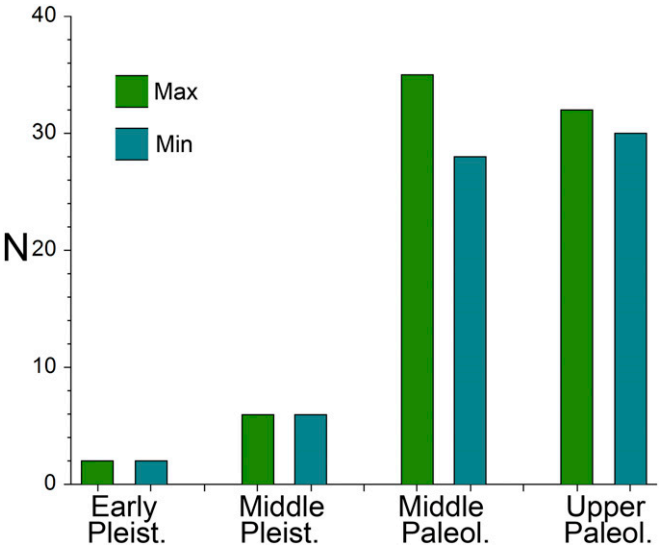

Fig. 2. The distribution of developmental abnormalities by period through the Pleistocene/Paleolithic. The Middle Paleolithic specimens are limited to the Late Pleistocene. The maximum (Max) samples are counts by abnormalities; the minimum (Min) samples reduce the counts by pooling the same variants in multiple individuals from the same level of a site. Paleol, Paleolithic; Pleist, Pleistocene.

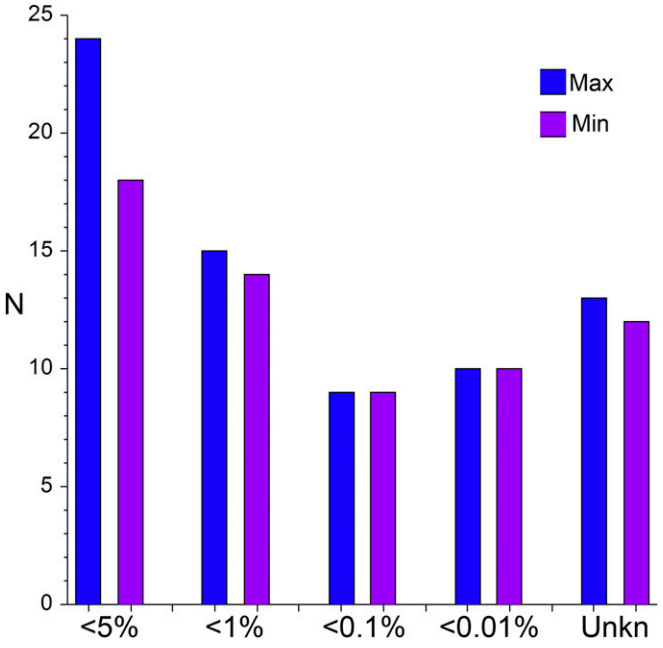

Fig. 3. The distribution of developmental abnormalities by their incidences in recent human samples or probabilities relative to appropriate paleontological samples (*SI Appendix*). Unkn., abnormalities with unknown etiologies. The maximum (Max) samples are counts by abnormalities; the minimum (Min) samples reduce the counts by pooling the same variants in multiple individuals from the same level of a site.

specimens (ones that are sufficiently complete to evaluate the presence of a given abnormality from the appropriate time period and/or geographical region) is less than a few dozen and often less than 10. This applies even to the relatively more common crania, mandibles, teeth, and femora. For examples with larger comparative samples, relative to the mandibular flanges of Palomas 6 and 23, there are 30 other Neandertal mandibles for comparison; for the Denisova and El Haroura M3s, there are 32 and 42 late archaic M^3s and M_3s, respectively, globally for comparison (and 28 and 20 Early/Mid Upper Paleolithic comparative M3s, respectively, for the Oase 1 and 2 M3s); for the Atapuerca-SH Cr.14 lambdoid synostosis, there are ∼25 sufficiently complete European Mid Middle Pleistocene crania (including 16 from Atapuerca-SH); for the Xujiayao 11 foramina parietalia permagma, there are 26 relevant Late Pleistocene archaic human parietal bones; and for the Sunghir 3 deformed femora, there are 37 sufficiently complete juvenile to adult femoral diaphyses from the European Early/Mid Upper Paleolithic (42 globally, three of which are abnormal, providing overall 9.3% unusual femora). The relevant comparative samples decrease markedly if restricted geographically or temporally and for other skeletal elements.

The probabilities of finding some of the rarer conditions, or the ones for which even a proximate etiology is unclear, are therefore extremely low given relevant Pleistocene human sample sizes. More importantly, the multiplicative cumulative probability of finding the 75 developmental abnormalities is vanishingly small. This statement holds even if the probability values are corrected for the relevant Pleistocene comparative sample sizes and the possibly related individuals from specific sites.

In addition, many of these abnormalities have been documented only in the past quarter century, as paleopathological assessments of the remains have become routine (see references in *SI Appendix*); additional ones are likely to be present in the currently available fossil remains. Regardless of the ultimate number of such abnormalities in the fossil record, it is apparent that the Pleistocene human fossil record is characterized by a plethora of developmental abnormalities, some relatively well known but others extremely rare. The probability of finding this density of rare developmental abnormalities in recent human samples of comparable size is, again, vanishingly small.

Discussion

The elevated incidence of rare to exceptional developmental abnormalities among Pleistocene humans raises questions regarding survival, mortuary behavior, levels of stress, consanguinity among these foraging populations, and possible trends through the Pleistocene.

Issues of Survival. The appearance of these skeletal and dental variations in the fossil record indicates some level of survival. Three-quarters of the individuals were mature, and the youngest survivors (Garba IV-E43, Grotte-des-Enfants 1, Pech-de-l'Azé 1, Rochereil 3, and Subalyuk 2) were 2–3 y postnatal (not including the Krems-Wachtberg neonates). Slightly older immature individuals with serious disorders, the hydrocephalic Qafzeh 12 and the Atapuerca-SH Cr.14 with cranial synostosis deformities, lived to 3–4 y and midjuvenile age, respectively. The survival of the youngest individuals into early childhood may have been facilitated by maternal care, but the persistence of individuals to late juvenile or older ages with serious developmental abnormalities in both the Middle and Late Pleistocene (e.g., Salé 1, Singa 1, Dolní Věstonice 15, Sunghir 3, Arene Candide 3, Romito 2) implies some level of social support (7, 8).

Issues of Mortuary Behavior. The presence of the developmentally (and degeneratively) unusual individuals in European Upper Paleolithic burials has suggested differing mortuary treatment of those individuals as a result of their unusual biologies (ref. 9; see also refs. 10–12). Among the 105 sufficiently preserved western Eurasian Upper Paleolithic burials, at least 8 (7.6%) exhibit developmental abnormalities that would have been evident to their kin. These individuals are Arene Candide 2 and 3, Barma Grande 2, Dolní Věstonice 15 and 16, Krems-Wachtberg 1-2, Romito 2, and Sunghir 3; to these cases can possibly be added Rochereil 1, Pataud 1 and Sunghir 2, increasing the percentage of Upper Paleolithic cases to 10.4%.

Although formal burials were present in the Middle Paleolithic, it is difficult to determine how many of the approximately 45 associated skeletons are from intentional burials (13, 14). In any case, only three (6.6%) of the possible Middle Paleolithic burials yielded remains with marked developmental abnormalities (Kebara 2, Qafzeh 12, and Regourdou 1). There is no convincing evidence of differential mortuary behavior before the Late Pleistocene.

Therefore, although there are a number of cases of pronounced developmental abnormalities from Upper and Middle Paleolithic burials, the overall percentage of externally apparent cases (≤9.3%) is sufficiently modest to make it unclear whether this pattern reflects the pan-Pleistocene levels of unusual biologies (and behaviors) at the time of death or differential mortuary treatment. The number of developmental abnormalities from isolated skeletal elements (Table 1 and *SI Appendix*), along with the relative abundance of developmental abnormalities before the early Late Pleistocene advent of intentional burial, suggest the former interpretation.

Issues of Stress. The abundance of developmental abnormalities among Pleistocene humans may have been enhanced by the generally high levels of stress evident among these foraging populations. Nonspecific stress indicators, principally dental enamel hypoplasias, are common among them (15–19). However, the overall frequencies of the lesions are within the ranges

Table 1. Individuals by rarity of lesion

Type	<5.0%	<1.0%	<0.1%	<0.01%	Unknown etiology	Unknown incidence
Systemic	Krems-Wachtberg 1-2	Cussac L2A	Qafzeh 12	Arene Candide 3 Romito 2	Dolní Věstonice 15 Sunghir 2	
Cranial		Dolní Věstonice 16 Pech-de-l'Azé 1 Salé 1	Arene Candide 12 Singa 1	AT-SH Cr.14 Pech-de-l'Azé 1 Xujiayao 11	Rochereil 3	
Mandibular					Palomas 6 and 23	
Dental	Lazaret 18/19	Dolní Věstonice 15 and 33	Denisova 4	Denisova 8		El Sidrón Adult 2
	Qafzeh 15 Zhiren 3	Garba IV-E43 El Haroura 1 Oase 1 and 2 Sunghir 2	Malarnaud 1 Pavlov 21 Subalyuk 2	Lazaret 18/19 Pataud 1 Pataud 6		El Sidrón Adol. 3
Vertebral	Kebara 2 Shanidar 1 and 4 Shanidar 3 (2) El Sidrón SD-1643 Taforalt 11 Villabruna 1	AT-SH Pelvis 1 Nariokotome	El Sidrón SD-1094		Arene Candide 2 Grotte-des-Enfants 1 Kebara 2 Rochereil 1	
Upper limb	Villabruna 1	Sunghir 1		Barma Grande 2		
Lower limb			Berg Aukas 1		Nazlet Khater 2 Regourdou 1 Sunghir 3 Tianyuan 1	Arene Candide 2
Hand/foot	Baousso da Torre 1 and 2 Krapina 200.1 Shanidar 3, 4, 6, 8 El Sidrón (4x)	El Sidrón SD-96				Dolní Věstonice 16
Total (max), n (%)*	24 (33.8)	15 (21.1)	9 (12.7)	10 (14.1)	13 (18.3)	4
Total (min), n (%)	18 (28.5)	14 (22.2)	9 (14.3)	10 (15.9)	12 (19.0)	3

See discussions in *SI Appendix* for each assignment. Note that some specimens are listed twice, given the presence of apparently separate anomalies/abnormalities. Adol, adolescent; AT-SH, Atapuerca-SH; Cr, cranium.

*The maximum total is by abnormality and individual; the minimum total counts individuals from one site level with the same abnormality as one, given possible shared genetic bases or predispositions.

of variation exhibited by late prehistoric samples of foraging populations (20), and the severe and persistent hypoplasias are mainly associated with other abnormalities (18, 19). Traumatic lesions are common, although the majority are minor cranial ones (1, 21). A few of the abnormalities may be posttraumatic, such as the L5 spondylolysis of Villabruna 1 or the lesser trochanter absence of Arene Candide 2, but it is unlikely that many (or any) of the other lesions were produced by trauma. Thus, it is difficult to account for more than a few of these abnormalities as the secondary products of stress during development.

Issues of Consanguinity. Several of these abnormalities are associated with genetic variants among extant humans (e.g., refs. 7 and 22–24), some which are expressed or more severe through homozygosity. Other anomalies (especially dental and vertebral variants) appear to have inherited predispositions, as shown primarily through family studies (e.g., refs. 25–30). Therefore, it is possible that the elevated frequency of these conditions is a product in part of high levels of consanguinity in Pleistocene populations (2, 31). Estimates for Pleistocene human population densities are generally low (32) and for effective population sizes are very low (33), implying high levels of inbreeding within local populations.

Morphological uniformities in at least some features within various human paleontological site samples suggest high levels of consanguinity (e.g., refs. 33–41), and the co-occurrence of developmental abnormalities in multiple individuals within sites reinforces these interpretations (refs. 31 and 42–46, *SI Appendix*). However, other sites exhibit considerable variation in skeletal features (e.g., refs. 12 and 47–51), making it uncertain to what extent these site and stratigraphic level samples were closely related.

Late Pleistocene human ancient DNA (aDNA) presents a similarly ambiguous picture. Three Neandertal sequences exhibit high levels of homozygosity, implying pervasive inbreeding among their ancestors (52, 53), and one Neandertal sample has provided low levels of genetic diversity, especially among males (54). The Neandertals have also been characterized as having low genetic diversity overall relative to recent humans (55). However, "Neandertal DNA" is known from Atlantic Europe to Siberia (51, 53), and all sampled early modern humans across Eurasia exhibit modest levels of Neandertal DNA (56–58), implying that there was a widespread Eurasian presence of an interconnected Neandertal-related population, a pattern also evident morphologically (59). Among early modern human site-specific samples, the aDNA evidence for consanguinity is equivocal, with variable degrees of within-site sample diversity (60–62).

Therefore, it is unclear to what extent the abundance of developmental abnormalities among Pleistocene humans could be due to a (necessarily pervasive given the wide temporal and geographical distribution of the abnormalities) high level of consanguinity. Both morphological and aDNA data present mixed perspectives.

Pleistocene Trends. As is evident in Fig. 2, the overwhelming majority (89.3%) of the identified anomalies/abnormalities are Late Pleistocene, with only two from the Early Pleistocene and six from the Middle Pleistocene. This contrast suggests a marked

increase in incidences later in the Pleistocene. However, before the advent of burial in the early Late Pleistocene, among both Neandertals and early modern humans, reasonably well-preserved and associated postcrania are very rare; they consist basically of KNM-WT 15000 and the Dmanisi and Atapuerca-SH samples (63–65), two of which provide anomalies. Pre-Late Pleistocene *Homo* crania frequently lack bases, dentitions are rarely complete, and vertebrae are limited to the same three sites. In addition, paleopathological assessments of Middle and Upper Paleolithic remains have a long history (*SI Appendix*), whereas only recently have similar concerns been raised with respect to the earlier remains. As noted above (see also ref. 66), differential survival of developmental and/or degenerative conditions is not likely to have changed markedly during the Pleistocene. It is therefore probable that the predominance of Late Pleistocene developmental abnormalities is a product of paleontological preservation and focus, rather than an increase in such conditions through the Pleistocene.

Conclusion

It is apparent that Pleistocene members of the genus *Homo*, from at least two examples in the Early Pleistocene to an abundance of cases in the Late Pleistocene, sustained and survived an elevated level of developmental abnormalities. Some of these developmental deficiencies are unexceptional from a recent human perspective, although finding multiple cases of them within and across samples and time periods suggests elevated levels of these more common patterns. However, one-quarter of the cases are rare (some extremely so) in extant human samples, and an additional one-fifth of the cases defy proper diagnosis. Only when this pattern and the associated implications of this high level of developmental anomalies and abnormalities are taken into account will it be possible to provide a comprehensive paleoanthropological assessment of human behavioral and populational processes through the Pleistocene.

Materials and Methods

The data consist of individual cases of developmental abnormalities, almost all of which have been previously documented in the literature and are summarized in *SI Appendix* with additional contextual information. These data have been summarized in terms of their incidences from the recent human literature or their probabilities relative to the appropriate human paleontological samples (Table 1). All details and references are provided in *SI Appendix*.

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