**S1 Text**

**Results of Additional Analyses**

*Cranium and Brain*

Head circumference: Falk et al. [1] first published a measurement of head circumference (HC; a proxy for brain size) of 39.4 cm. Henneberg et al. [2] provided a similar measurement of 38.5 cm and then estimated HC in the local Rampasasa population from its average endocranial volume (EV) by a linear regression equation developed from adult Aboriginal Australians. From the 95% confidence interval of 450-522 mm, and a SD of 20.5 mm based on the Australian sample, they determined LB1 HC to be -3.17 to -6.68 SDs below the Rampasasa range. They argued that this range was comparable to the deviation of HCs in a sample of DS children (15 mo to 13.9 y) from same-aged population averages found in Castells et al. [3]. We find this approach unnecessarily convoluted. Head circumference data are available for adult individuals with DS. For example, Tüysüz et al. [4] presented a growth curve for Turkish females with DS from ages 3-18 years. At age 18, the 97th, 50th and 3rd percentiles are 54.2, 51.3 and 48.6 cm, respectively. By comparison, the LB1 soft tissue values (estimated from the osteological measurements using the formula provided by Henneberg et al. [2014]) are 42.2 based on Falk et al. [1] and 41.3 cm based on Henneberg et al. [2], both well below even the 3rd percentile of estimated HC for DS. Comparable data were not available for Indonesian populations. In addition to the much smaller brain size of LB1, the shape of the LB1 endocast is distinct when compared visually with the virtual endocasts from the six DS females in our sample and six non-DS females (S1 Fig).

**S1 Fig. Right-lateral (A) and anterior (B) views of virtual endocasts for six Euploid females from a previous study [5], LB1, and our six subjects with DS.** All virtual endocasts are scaled to size.

Cranial asymmetry in Down syndrome: It has been hypothesized that trisomy 21 causes "amplified developmental instability" and increased variance of phenotypic characteristics [6-8]. Developmental instability (DI) refers to an organism's tendency to produce a morphological change in response to developmental perturbations. Proponents of the hypothesis that Down syndrome is a case of amplified developmental instability argue that trisomy 21 causes a generalized genetic imbalance that disrupts evolutionarily conserved developmental pathways by decreasing developmental homeostasis and precision.

Historically, DI has been estimated as a measure of the metric differences between the left and right sides of symmetrically developing organisms (i.e., fluctuating asymmetry). Since in typically developing symmetric organisms, the left and right halves experience the same environmental and genomic influences during development, bilateral features are expected to develop as mirror images of the opposite side. According to this model, the developmental program of any organism is driven genetically and buffered or canalized in such a way that development tends to proceed along evolved trajectories unless perturbed by environmental or genetic insult. Genetic or environmental stress during development can increase developmental noise, expressed as minor departures from an ideal developmental program of perfect bilateral symmetry. While symmetry is a property of the individual, patterns of asymmetry for specific traits are studied at the level of the population [9-12].

Starbuck et al. [13] tested a hypothesis of developmental instability in DS by estimating fluctuating asymmetry in the 3D morphology of soft tissue facial features in children with DS and found that parts of the face in individuals with DS, especially those derived from the mandibular prominence of the first pharyngeal arch, showed increased developmental instability as measured by fluctuating asymmetry relative to carefully chosen comparative (euploid) samples. Henneberg et al. [2] used the correspondence between their facial measures of asymmetry in the LB1 specimen and the soft tissue facial features evaluated by Starbuck et al [13] as support for the diagnosis of DS. However, these two sets of measurements are not commensurate. The data from LB1 were measures of directional asymmetry in osteological features from a single fossil [14], not measures of fluctuating asymmetry in soft tissue features measured across a sample.

*Dentition*

The clinical literature regarding oral health issues (related to both hard and soft tissues) is extensive. While occlusal issues related to the underdevelopment of the maxillae are common, the frequency and expression of other traits is highly variable and no traits are DS specific. Although, they ignore the larger set of dental traits more often associated with DS [15] (S1 Table), with evidence preserved in the teeth and dental arches of LB1 and LB6, Henneberg et al. ([2]: SI) argue that the presence of periodontitis, a low caries incidence and possible evidence of taurodontism in LB1 *H. floresiensis* is consistent with DS.

Periodontal disease: A higher frequency of periodontal disease has been documented for DS patients than in age-matched controls, with prevalence rates as high a 58% of individuals 9-39 years being reported, versus ~20% of the control group [16]. The etiology of this is uncertain, but factors of poor oral hygiene, immunological deficiency, impaired masticatory function and salivary deficiency have been proposed [17,18]. Evidence of periodontal disease in LB1 includes heavy dental calculus and alveolar recession in the posterior dental arch of the mandible and maxilla [19]. There is no evidence of periodontal disease in the LB6 mandible.

Periodontal disease in LB1 has previously been discussed in Brown and Maeda [19], with calculus deposits and alveolar bone erosion associated with the posterior teeth. The formation of static plaque deposits and calculus is multifactorial, and periodontal disease is common in pre-Neolithic and post-Neolithic human populations [20,21], some species of wild primates [22,23], and has been recorded in hominins as diverse as South African australopiths [24] and *Homo* *antecessor* [25]. In wild, non-carnivore, mammals, the frequency of periodontal disease is linked to diet [26], with heavy tartar deposits in foliverous colobines [23]. While the presence of infant Stegodon in the Pleistocene deposits associated with *H. floresiensis* at Liang Bua, suggests the seasonal consumption of some meat, there is no direct evidence of the vegetative component of the diet [19]. The reasons for the adherence of calculus deposits in LB1 remain unknown, but are likely to involve both oral physiology and diet. By itself, and in the absence of numerous other dento-facial indicators (S1 Table), the presence of periodontal disease in LB1, but not LB6, adds very little to a differential diagnosis of DS.

Caries: Although they have previously indicated that they believe that tooth loss in LB1 (LB1 right P2, right M3) was the result of caries [27], Henneberg et al. ([2]: Table 1, SI) argue that a low caries incidence in LB1 and LB6 is consistent with DS. In general, DS children appear to have a lower caries incidence than reported for their unaffected siblings [28]. Although minimal tooth wear has usually preserved the fissures and crevices on their occlusal surfaces, it seems that the oral environment in DS children is not conducive to the adherence of *S. mutans* biofilms and fermentation of caries producing lactic acid [18]. This contrasts with a low caries incidence in recent hunter-gatherers, and Pleistocene hominins, that is associated with heavy tooth wear and diets low in fermentable carbohydrates [29,30,31]. There is no evidence of caries in LB1, or the LB6 mandible, and the pattern of tooth wear, on both the occlusal and interproximal surfaces, is consistent with that in hunter-gatherers and Pleistocene hominins [19,32,33].

Taurodontism: In 2008 Obendorf et al. [34] argued that the Liang Bua *H. floresiensis* skeletons were most likely the remains of modern humans with myxoedematous endemic (ME) cretinism. They also claimed to see evidence of taurodontism in the LB1 and LB6 teeth in “captured images from X-ray scans presented in The mystery of the human hobbit (BBC Horizon, 2005)” ([35], p. 1290; [36]). Some of these images can be seen in S2 Fig.

Taurodont molar teeth have a vertically enlarged pulp chamber, with apical displacement of the pulpal floor, no constriction at the level of the cement enamel junction, the point of trifurcation/bifurcation of the roots is moved apically, and there is greatly reduced vertical root length Third molar teeth are more commonly affected than the first and second molars, both deciduous and permanent teeth can have taurodont pulp chambers [37] and permanent premolars can also be taurodont [38]. Taurodont teeth are known to occur at high frequency in a range of x-linked syndromes [39,40], DS [41,42], Klinefelter’s Syndrome [43], and at a lower frequency in the human population more broadly, although some modern human populations have higher frequencies of taurodontism than others [44,45]. For instance, a high frequency of taurodontism has been described for at least one Australomelanesian population, the Broadbeach burials [45] [contra 2]. Taurodont permanent and deciduous teeth are also known to occur at a high frequency in Neanderthals [46], for instance at Krapina [47], and in Zhoukoudian *H. erectus* [48], without any associated skeletal evidence of developmental syndromes.

Henneberg et al. ([2], Table 1, SI) revisit the subject of taurodontism in the Liang Bua hominins, using this as possible support for their DS diagnosis. They write, “Others (Obendorf et al. 2008) have proposed the presence in LB1 of **“**significant taurodontism; that is, the presence of an enlarged tooth body due to an apical displacement of the root bifurcation, is evident in these and other LB1 teeth.… we regard the presence of some degree of taurodontism in LB1 as sustainable. Its presence is, however, uncertain due to the poor quality of evidence that continues to be provided by Peter Brown and his supporters.”

However, micro CT scans of the LB1 mandibular first molars demonstrate that they are not taurodont [33,36]. Similarly, radiographs of the LB6 mandible demonstrate that the M1’s have normal pulp and root dimensions, but shadows from antimeres obscure these details in the other molar teeth (S2 Fig).

**S2 Fig. Lateral radiographs of LB6 posterior teeth and tooth roots.** Both images show that the M1 (indicated by the arrow) is not taurodont.

*Postcranial anatomy*

Humerus:Femur ratio: Henneberg et al. [2] asserted that the femur was short relative to the humerus in LB1 and individuals with DS. They based this on data on growth in Indian children with DS (6-18 y) and anthropometric measurements of the thigh and upper arm from Smith and Ulrich [79] on matched adult DS and euploid samples. However, the average ratio was actually lower in DS than the matched controls in the adult dataset from Smith and Ulrich [79], which indicated that, if anything, the arm was disproportionately short rather than the leg in DS (SI Fig 3). Moreover, the ranges for the anthropometric (soft tissue) ratios (raw data from Ref. [79] provided by E. Smith) are inflated relative to the skeletal measures and likely incorporate a high degree of measurement error. In fact, the range of soft tissue values for the control (euploid) sample subsumes the equivalent measures for the DS sample as well as the skeletal ranges for 1 average-sized and 4 small-bodied modern humans groups. The LB1 value of 86.8 is considerably higher than the average values for both the skeletal and anthropometric ratios reported for the euploid and DS groups and well beyond the range documented for DS. Together, these observations suggest that 1) the available data for upper arm:thigh ratio do not discriminate between the DS and the control group and 2) LB1 is likely an outlier with respect to both groups, but skeletal ratios for DS would be necessary to confirm this.

**S3 Fig. Humerus: femur (skeletal) and upper arm: thigh (anthropometric) ratios of euploid and DS samples as well as LB1.** The five samples on the left represent one average-sized (Zulu) and four small-bodied populations of euploid humans. The ratios for the DS and control samples on the right were based on soft-tissue measurements from a clinical study [79]. The box-and-whisker plots include the average, +/- 1 standard deviation and range (extreme outliers indicated by circles).

Digit length: Additional comparative data on absolute and relative phalangeal length from a cadaver sample of average body size are provided in S2 Table to complement the smaller dataset derived from small-bodied populations in Table 3 of the main text.

Atlantoaxial or atlanto-occipital instability. Atlantoaxial and atlanto-occipital (or craniocervical) instability and hypermobility have been reported for DS, but are difficult to assess reliably radiologically [80]. Both are usually attributed to ligamentous laxity (which is pervasive in patients with DS) (e.g., [81]) as much of the stability of these joints is through soft tissue mechanisms. Bony abnormalities sometimes associated with atlantoaxial instability are hypoplasia of the C1 arch, basilar invagination and os odontoideum [80]. Flattening or hypoplasia of the occipital condyles can create a “rocker bottom” which also contributes to atlanto-occipital instability [82,83].

Henneberg et al. [2] described LB1 as having an “atlanto-occipital abnormality” and cited the work of Kaifu et al. [84] who described the right occipital condyle of LB1 as slightly concave and bearing a depression on its posterior portion, along with a roughened articular surface of the corresponding superior articular facet of C1. Kaifu et al. [84] interpreted this irregular anatomy as indicative of ***limited*** mobility (rather than instability and hypermobility), possibly from asymmetrical insertion of the nuchal muscles or congenital torticollis. Regardless of its interpretation, this description of the occipital condyle does not correspond to the “rocker bottom” anatomy sometimes seen in atlanto-occipital instability, although we could not locate any photographs with which to compare the LB1 condition. Therefore, while there is an “abnormality,” there is no evidence that this corresponds to the specific anatomical anomaly seen in some individuals with DS.

Feet: The “flat foot” feature identified by Henneberg et al. [2] in LB1 and in DS is comparable in name only. Flat foot (pes planus or pes valgus) is found in 60-70% of pediatric DS patients aged 4-10 years [85], which is higher than values reported for similarly aged non-DS children (24-40%) [86,87], and adults with DS (20%) [88]. Most cases of flat foot in DS are categorized as flexible flat foot, which refers to the loss of the medial (longitudinal) arch of the foot during weight support, often accompanied by pronation of the foot. This is again likely related to ligamentous laxity in DS [89]. Rarely flat foot in DS results from vertical talus (0.7%; [88]) which is characterized by a dislocation of the navicular dorsally on the talus, a talus that is waisted (hour-glass shaped), a calcaneus that narrows anteriorly and is beak-shaped, and a navicular that is wedge-shaped on its plantar side [90,91]. Other common foot anomalies in DS include metatarsus primus varus (40% of children) and hallux valgus (26%), or both (34%) [85] which may be related to the common clinical finding of a wide gap between the first two toes (“sandal gap”).

The talus and navicular (but not the calcaneus) are preserved for LB1 and do not show evidence of vertical talus [92,93]. The flexible flat foot seen in DS could not be assessed in LB1 as this is not a bony deformity, but rather relates to ligamentous laxity. LB1 has been described as having a “flat foot” in the sense of a phylogenetically primitive architecture that is also seen in apes, some australopiths and possibly early *Homo* [92,93]. This interpretation hinged primarily on the large medial navicular tuberosity and lateral wedging of the navicular in LB1 which is generally interpreted as weight-bearing in apes and other fossil hominins that exhibit this feature [94]. There was no discussion of a large navicular tuberosity associated with DS in the clinical literature.

Metatarsus primus varus is identified when the intermetatarsal angle between the first two metatarsals is >9⁰ [95]. Alignment of the articular surfaces of the medial cuneiform and first metatarsal (first tarso-metatarsal joint) indicate that the first metatarsal is fully adducted and in line with the other metatarsals [92] in contrast with the expected abduction that defines metatarsus primus varus. Hallux valgus is identified when the hallux valgus angle exceeds 15⁰ [95]. This could not be evaluated for LB1 as the 1st proximal phalanx was not preserved. However, these two conditions are associated and often co-occur [95,96].

The presence of osteophytes in two proximal pedal phalanges was used as supporting evidence for flat foot in LB1 [2]. It is difficult to know the etiology of these osteophytes as they are a common feature of osteoarthritis which is influenced by many factors [97]. It may be the case that the flat foot of LB1 impacted their development. This is not, however, support for a DS diagnosis because the phylogenetically primitive traits leading to flat foot in this individual are very distinct from the flexible flat foot found in DS. Osteophytes could also be a result of trauma.

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