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3 **Postnatal changes in the growth dynamics of the human face revealed from the bone**

4 **modelling patterns**

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22 **Abbreviated title:** Postnatal bone modeling in the human face

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## INTRODUCTION

The skull is an anatomically complex system, which has been a focal point for studies in vertebrate biology for more than a century. It presents unique opportunities to examine the role of the multiple, intricate developmental processes involved in the craniofacial morphology and in the evolutionary origin of the hominid cranium. Understanding the development of the skull can be achieved through the study of the growth dynamics of their skeletal elements considering the Moss' functional matrices theory (Moss and Young 1960; Moss 1962; Moss, 1970 c, d; Moss and Salentjin, 1969) and the Enlow's counterpart principle (Enlow et al 1969; Enlow and Hans, 1996). According to this theoretical framework, the human craniofacial skeleton results from the interactions of their different components that are influenced by both internal (e.g. hormonal and genetic factors; e.g. Enlow and Hans, 1996; Moss, 1960) and external stimuli (soft tissue growth, dental maturation, biomechanical factors; e.g. Moss and Young, 1960; 1997a,b,c,d; Moss and Young, 1960; Moss and Rankow, 1968; Atchley and Hall, 1991; Enlow and Hans, 1996; Lieberman et al.,2002; Klingenberg et al., 2003). The growth of the skeletal elements involves changes in their size and shape as well as their relative position within the craniofacial system in order to maintain the proper bone alignment, function and proportionate growth (e.g. O'Higgins et al., 1991; Enlow and Hans, 1996; McCollum, 1999). During the human development, these skeletal elements from the neurocranium, viscerocranium and mandible are intimately associated to the functional spaces (cranial, orbital, nasal, and oral cavities) and the soft tissues in which they are embedded (e.g. brain, muscles, connective tissues) (Moss and Young 1960; Moss, 1962; 1997a; Enlow and Hans, 1996).

The skull grows through two simultaneous and interrelated processes: growth modelling and growth displacements of the skeletal elements. Growth modelling consists in the coordinated activity of two cellular groups, osteoblasts forming bone on one surface and

osteoclasts removing bone in the opposite surface (Enlow, 1962; Bloom and Fawcett, 1994; Enlow and Hans, 1996). This mechanism results in the increase in size of the bone and the growth movement in the direction of the forming bone surfaces also termed cortical drift (Enlow, 1962; 1963; Enlow and Harris, 1964). As a consequence of the bone modelling growth, the skeletal components are displaced into the craniofacial system with coordinated and passive movements -the primary and secondary displacements- as well as rotations (for a detailed description of these movements see Björk, 1969; Moss and Young, 1960; Moss, 1970; Bjork and Skieller, 1972; 1976; Enlow and Hans, 1996).

In the last century, Enlow showed that the activity of osteoblasts and osteoclasts is recorded in the bone surface (last formed bony lamellae) as fields of growth activity,bone formation and resorption fields (Enlow, 1963; Enlow and Hans,1996). The distribution of these growth fields –the bone modeling pattern– is species-specific and its interpretation following the craniofacial biology principles provide data on the growth dynamics of the craniofacial skeletal components during human ontogeny (e.g. Enlow and Harris, 1964; Mauser et al., 1975; Kurihara et al., 1980; Enlow and Hans, 1996; McCollum, 2008). According to these studies, the prenatal craniofacial system shows a general growth as indicated by the bone deposition surfaces (Mauser et al., 1975; Enlow and Hans, 1996; Radlanski and Klarkowski, 2001). Bone resorption activity is first reported in the mandibular corpus and ramus around $8,5^{th}$-$9^{th}$ prenatal weeks (Radlanski and Klarkowski, 2001; Mauser et al., 1975; Enlow and Hans, 1996) indicating a lateral growth of the mandibular corpus and a posterior relocation of the ramus (Mauser et al., 1975; Enlow and Hans, 1996). In the postnatal period, the human facial skeleton is depository until 3 months of age, when bone resorption surfaces appear in the nasoalveolar clivus (Kurihara *et al.*, 1980; Enlow and Hans, 1996; McCollum, 2008). From 2 to 14 years old, resorbing activity spread out over the nasomaxillary region although the extension and the location of resorbing fields change

77   throughout ontogeny indicating changes in the growth dynamics associated to downward

78   growth of the human face (Kurihara et al., 1980; McCollum, 2008). Postnatal changes in the

79   bone modeling activity are also observed in the human mandible (Enlow and Harris, 1964;

80   Kurihara et al., 1980; Hans et al., 1995). At 2 years old, bone resorption fields appear for the

81   first time in the alveolar region of the buccal symphyseal region. From this age to 14 years

82   old, resorption extends towards the basal area of the symphyseal region and/or through the

83   anterior area of the mandibular corpus (Kurihara et al., 1980). During this postnatal period,

84   the mandibular ramus shows a complex modelling pattern indicating a posterior growth of the

85   mandible and its anterior displacement (Enlow and Harris, 1996). These studies analysed

86   facial skeleton growth up to 14 years old but the bone modelling activities during the

87   adulthood period remains almost unstudied. The aging craniofacial skeleton and mandible

88   show morphological changes related to their horizontally increase in size of the maxilla and

89   the mandible and to their increase in height of the anterior face (e.g. Behrents, 1985; Forsberg

90   et al., 1991; Bishara et al., 1994; Enlow and Hans, 1996; Bondevik, 1995; Doual et al., 1997;

91   West and McNamara, 1999; Akgül and Toygar, 2002; Albert et al. 2007; Williams and Slice,

92   2010; Tsiopas et al., 2011). In the present study, we analyse the postnatal growth dynamics of

93   the craniofacial skeleton comparing juvenile and adult specimens. We observe that adult and

94   juvenile specimens show different bone modelling patterns, adults presenting an increase of

95   bone formation surfaces in the maxilla and mandible that explains the horizontal and vertical

96   changes observed in aging craniofacial skeleton.

97        In addition, we explore how modelling activities of the facial skeleton and mandible

98   regions are related during the ontogeny. As mentioned above, the skeletal components

99   growing within the craniofacial complex system interact with each other keeping a functional

100  and structural balance whereas they increase in size during development (Enlow and Hans,

101  1996; Moss and Young, 1960; Moss, 1962). Correspondences between different anatomical

102    parts of the skull have been demonstrated by morphometric analyses (see Bastir *et al.*, 2006).

103    However, previous studies on the craniofacial growth through the analysis of modelling

104    activities have focused on particular facial or mandibular regions, except for Enlow's

105    reference work on craniofacial morphology in individuals up to 14 years old (Enlow, 1982,

106    revised in Enlow and Hans, 1996). In the present study, we hypothesize that ontogenetical

107    changes of the bone modelling also reflect the relationships between the facial and mandible

108    skeleton to maintain the functional and physiological balance of the craniofacial system.

109    Results obtained in this work will allow us to hypothesize how these relationships could be

110    involved in the morphology of the human skull.

111

112    **MATERIAL AND METHODS**

113    The sample analysed in this study comprises twelve human skulls of known age and

114    sex divided into two subgroups: 6 specimens in the subadult group and 6 specimens in the

115    adult group (Table 1). All specimens belonged to the Anthropological Collection of the

116    University of Coimbra (Portugal). Individuals with malformations, traumatisms, or alveolar

117    bone resorption caused by tooth loss during life were excluded.

118    Obtaining the bone modeling pattern requires the microscope analysis of the bone

119    surface to identify bone formation and resorption fields. The best preserved half part of both

120    facial skeleton and mandible was employed in the analyses. We have used a non-destructive

121    methodology that involves the replication of the bone surface and the microscope analysis of

122    these replicas (Martinez-Maza et al., 2010; see also Bromage, 1989). Specimens were first

123    cleaned with 60% alcohol applied with a smooth hair brush to eliminate any particles

124    adhering to the microrelief of the bone. Second, the negative impressions of the periosteal

125    bone from the facial skeleton and the mandible were made using a low-viscosity silicone

126    (Exaflex injection type 3 low viscosity; DVD Dental, SA, Spain). Negative impressions were

127  made independently from anatomical regions of the facial skeleton (glabella, superciliar arch,

128  nasal bones, naxomaxillary region, zygomatic bone) and the mandible (buccal and lingual

129  side of the symphysis, mandibular corpus, and ramus) to fit the microscope's size limitations

130  and to facilitate the manipulation during observation. Once silicone was cured, the negative

131  cast was removed from the bone surface and delimited with a retaining wall elaborated with a

132  silicone Optosil P plus and Optosil Xantopren (DVD Dental SA, Spain). Finally, positive

133  replicas of each anatomical region were generated using the polyurethane resin Feropur

134  (Feroca, SA, Spain). Replicas were then coated with gold (sputter coater SC510 BIORAD)

135  prior to observation under a reflected light microscope (Olympus BX51TRF microscope

136  equipped with an Olympus DP11 digital camera) using a 20 X objective (Martinez-Maza et

137  al., 2010). To facilitate the localization of the remodeling microfeatures of the bone surface, a

138  grid of 5X5 mm squares was drawn on the surface of the gold-coated replica using a sharp

139  permanent pen. Each square was referred to by a coordinate (x,y) starting on the inferior left

140  square (1,1). This grid and the outline of the anatomical region were drawn on a paper to

141  record the data from the microscope.

142      The microscope analysis of the replicas from the periosteal bone surfaces allowed us

143  to identify and map the fields of growth modeling activities following the criteria provided by

144  Martinez-Maza et al. (2010; see also Bromage, 1989). Briefly, bone forming surfaces are

145  characterized by mineralized collagen fibre bundles produced by osteoblasts (Figure 1a;

146  Boyde, 1972; Bromage, 1989; Martinez-Maza et al, 2006; Martinez-Maza et al., 2010) and

147  bone resorbing surfaces showed Howship's lacunae produced by the osteoclasts (Figure 1b;

148  Boyde, 1972; Bromage, 1989; Martinez-Maza et al., 2010). Bone surface also showed eroded

149  surfaces characterized by several marks associated to the manipulation of the skulls such as

150  trampling, tool marks, fissures or writing marks, where neither bone formation nor resorption

151  features could be identified. From these data, modelling patterns for each individual were

152    drawn. Following previous works, generalized modeling patterns for the subadult and the

153    adult groups were established through the identification of intraspecific similarities in the

154    bone modeling field distribution of each anatomical region of the facial skeleton and mandible

155    (Enlow and Hans, 1996; Bromage, 1989; Rosas and Martinez-Maza, 2010; Martinez-Maza et

156    al., 2011).

157

158    **RESULTS**

159        Schematic bone modeling maps of subadult and adult specimens analysed in this study

160    are represented in Figures 2 and 3. Individual patterns show bone modeling fields with

161    variable size and shape, irregular boundaries, and patchy distribution. Even though different

162    specimens show eroded surfaces lacking information, histological data recorded from the

163    facial and mandibular regions have allowed us to elaborate generalized bone modeling

164    patterns for adults and subadults (Figure 4). A detailed description of the modeling fields

165    identified in the facial skeleton and the mandible is provided. Finally, we compare the

166    generalized bone modeling patterns of subadult and adult groups.

167

168    *Facial skeleton: subadult specimens*

169        The upper region of the facial skeleton (glabella and superciliar arch) is mainly

170    depository. Small resorption fields are only found in the superciliary arch-glabella contact

171    area close to the frontonasal suture in individuals 101 and 218, and in the inferior area of the

172    superciliary arch of specimen 100A. In the nasal bones, depository surfaces are present in all

173    specimens but in 126 and 100A, which present resorptive fields close to the pyriform

174    aperture. The nasomaxillary region shows high variability in the distribution of modeling

175    fields respect to other facial regions. This region displays predominantly resorptive surfaces in

176    the maxillary bone and depository surfaces in the nasal or frontal processes in individuals 218

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177    and 101. This last specimen also presents small bone formation fields in the canine fossa

178    region close to the infraorbital foramen and in the lateral margins of the nasal aperture.

179    Specimen 100 shows bone resorption both in the nasomaxillary bone and in the nasal process,

180    while tiny depository surfaces are found close to the frontonasal suture and two fields in the

181    alveolar region of the maxilla. Specimens 284 and 126 show similar patterns characterized by

182    bone formation fields in the nasal process, in the lateral margins of the nasal aperture, in the

183    zygomaticomaxillary suture, and small depository fields in the canine fossa area. On the

184    contrary, specimen 100A shows mainly depository surfaces both in the nasal process and in

185    the maxillary bone, while resorptive surfaces are found close to the lacrimal area, in the lateral

186    margins of the nasal aperture, in the canine fossa area, and in the zygomaticomaxillary suture.

187    The zygomatic bone in all specimens displays primarily depository surfaces but three

188    specimens show bone resorption activity in the orbital margin of the frontal process either

189    close to the glabella (specimen 100) or extending from the zygomaticomaxillary suture to the

190    level of the infraorbital foramen (specimens 126 and 100A).

191    *Facial skeleton: adult specimens*

192          The bone modeling map of the upper facial region is characterized by bone formation

193    surfaces. Both the glabella and the superciliar arch regions are entirely depository in specimen

194    52, whereas specimens 92, 98, 144, and 342 show bone resorption fields in the glabella and in

195    the area between the glabella and superciliar arch and even in the frontonasal suture

196    (individuals 92 and 144). The remaining specimen (46) shows eroded bone surfaces in most

197    of the glabella and superciliar arch regions but small resorption fields are identified in the

198    glabella-superciliar arch region, and tiny bone formation fields can be identified in the

199    frontomaxillary suture and in the upper region of the superciliar arch. The nasal bones are

200    characterized by bone formation surfaces. This region is entirely depository in specimens 46

201    and 342, while in specimens 144 and 52 small resorptive fields are observed close to the

202 pyriform aperture and in the frontonasal suture area (specimen 144).  On the contrary,

203 specimens 92 and 98 show predominantly bone resorption fields of variable size. The nasal

204 process of the nasomaxillary bone is also characterized by bone formation surfaces occupying

205 the whole area in specimens 98 and 342, while specimens 46, 92, 52, and 144 show small

206 resorption fields in the area between the frontal process and the maxillary body, and

207 distributed from the orbitary lateral margin to the lateral margin of the nasal aperture. The

208 specimen 144 also displays resorptive surfaces along the lateral orbital margin. The studied

209 specimens display a highly similar distribution of the growth fields in the maxilla. This facial

210 region is predominantly depository with bone resorption fields extending from the infraorbital

211 foramen to the canine alveolus (46, 92, 98, 342, and 52). Small resorbing surfaces are also

212 observed close to the nasal process in specimens 46, 52, 144 and 92, in the zygomatic

213 nasomaxillary suture (specimens 46 and 92), and in the lateral-inferior margin of the nasal

214 aperture (specimens 144 and 52). On its part, the zygomatic bone shows some variability,

215 being mainly depository in specimens 46, 98, 52 and 342, while in specimens 92 and 144

216 bone formation is reduced to the infraorbital foramen area. Resorption fields are observed in

217 the zigomatic maxillary suture in individuals 46, 92 and 98, also along the inferior margin of

218 the bone zygomatic to the temporal zygomatic suture  in 92 and 98, and in the area extending

219 from the zigomatic maxillary suture to the infraorbital foramen level in specimen 46. The

220 specimen 92 displays bone resorption activity along the lateral orbital margin to

221 frontozygomatic suture. In this suture a resorption field is also observed in the specimen 144.

222

223 *Mandible: subadult specimens*

224 Among subadults, bone modeling activity is preserved in the mandibles of specimens

225 284 and 126, whereas specimens 101, 100A, 126, and 100 present a combination of eroded

226 surfaces and modeling fields with variable size and distributed along different mandibular

227     regions. In the symphyseal region, specimens 284 and 126 display predominantly bone

228     formation fields from the alveolar process to the inferior symphyseal border, whereas the

229     specimen 100A shows small depository fields in the mental fossae at the level of the central

230     incisives. All specimens show bone resorption fields in the alveolar process of the buccal side.

231     Small resorptive fields are also observed above the mental protuberance and at the level of the

232     canine in specimens 101 and 100A and in the mental fossae in individuals 100, 126, and 218.

233     The lingual side of the symphyseal region is characterized by depository fields distributed

234     both in the alveolar process and in the basal component in specimens 284, 126, and 101,

235     whereas depository fields of variable size are observed in the lingual alveolar process of

236     specimens 218 and 100, in the sublingual fovea of 100 and 100A, and in the inferior border of

237     specimen 100. Resorptive fields are restricted to the alveolar process of specimen 218, the

238     sublingual fovea of specimens 101 and 284, and the inferior border of specimen 284.

239     Subadult mandibular corpus is characterized by depository surfaces in the buccal side

240     and resorbing surfaces in the lingual side. However, some resorbing fields are found in the

241     buccal side in the alveolar process at the level of the second premolar in specimens 100A and

242     284, and in the basal component in the anterior region of the corpus of specimen 101, close to

243     the mandibular foramen in specimens 101 and 126, in the posterior region of the corpus in the

244     oblique line area of specimens 284 and 100A, and in the inferior region as a stripe of small

245     resorptive fields extending from the symphyseal region to the ramus of specimens 100A. On

246     its part, specimen 100 shows a high degree of erosion, but preserves resorption surfaces in the

247     alveolar process at the level of the incisives and the canine and close to the anterior border of

248     the ramus. At the lingual side, the sublingual fossa is characterized by bone resorption fields

249     in the premolar and molar area in specimens 218, 101, and 284 and in the molar region of

250     specimens 100 and 100A. Conversely, all specimens display depository surfaces in the

251     anterior area of the sublingual fossa at the level of the lateral incisives and the canines, from

252   the alveolar process to the mylohyoid line. The submandibular fossa is also characterized by

253   depository fields in specimens 101, 284, 100, and 100A, while erosion precluded obtaining

254   histological data from specimen 218. The lingual side of specimen 126 show a particular

255   modeling pattern characterized by bone formation surfaces in the sublingual fossa, whereas

256   the submandibular fossa is predominantly resorptive with depository fields at the level of the

257   first premolar and second molar.

258         In the mandibular ramus, the buccal side is predominantly depository in specimens

259   218, 101, 284, and 126, whereas in specimens 100 and 100A this region is characterized by

260   bone resorption surfaces. The bone formation activity in the specimens 218, 101, 284, and

261   126 is distributed as large (284 and 126) or small (218 and 101) fields throughout the buccal

262   side of the ramus. Among them, specimens 101, 284, and 126 display resorbing fields in the

263   anterior border of the ramus, the coronoid process and the condyle neck, and also, in the

264   specimen 284, bone resorption fields extend as a diagonal stripe from the coronoid until the

265   angle of the ramus. The remaining two specimens -100 and 100A- are characterized by

266   resorbing surfaces although bone formation is observed in the area between the coronoid

267   process and the condylar neck, and, in the specimen 100A, close to the angle of the mandible.

268   In the lingual side of the ramus, bone resorption activity predominates. Resorption fields

269   appear in the area between the anterior border and the endocoronoid crest of specimens 218,

270   284, 100, and 126, along the posterior region from the condyle neck to the angle of the ramus

271   in individuals 218, 101, and 126, and in the area associated to the pterigoideus internus from

272   which extend to the mandibular corpus in all specimens except in specimen 100. Depository

273   surfaces are observed close to the mandibular foramen between the condyle and the coronoid

274   in specimens 218, 101, 284, and 126, and in the corpus-ramus contact area of specimens 101,

275   284, and 126. Three specimens -284, 100, and 126- also display small depository fields below

276   the mandibular foramen and in the mylohyoid groove.

277 *Mandible: adult specimens*

278       The symphyseal region shows resorptive fields in the alveolar component of the
279 buccal side of specimens 46, 92, and 144, whereas specimens 52, 98, and 342 display
280 predominantly bone formation fields. The basal component of this region is always
281 depository, although specimen 342 also presents small resorbing fields at the mental fossa.
282 Similarly, the lingual side is characterized by depository surfaces in the alveolar process, but
283 specimens 46, 52, 98, and 144 also show small resorptive fields. The lingual basal component
284 of the symphysis mainly displays bone formation fields with resorptive fields in the mental
285 spine and in the digastric fossa regions.  In specimens 52, 92, 98, and 144 resorptive activity
286 is also identified in the sublingual fossa.

287       The mandibular corpus is predominantly depository. In its alveolar component, bone
288 resorption activity is just found at the level of the canine of specimen 46, the premolar of 92,
289 and the molar regions of specimens 92 and 98. On the other hand, the basal component of the
290 corpus displays small resorptive fields close to the mental foramen area in specimens 46 and
291 342, in the contact region between the mandibular corpus and the ramus in specimens 46, 92,
292 98 and 144, and as a large stripe of resorptive fields along the inferior region of the corpus
293 from the premolar area to the ramus in specimens 98 and 144. In the lingual side of the
294 corpus, specimens 46, 52, and 342 display depository surfaces in the anterior region of the
295 sublingual fossa extending from the symphyseal region to the premolar region. Small
296 depository surfaces are also identified in the molar region close to the mylohyoid line of all
297 specimens but 342, and in the alveolar component of specimens 92, 98, and 144. The
298 premolar-molar region of the sublingual fossa of all individuals is characterized by bone
299 resorption fields. The submandibular fossa displays depository surfaces along the mylohyoid
300 line area and throughout the molar area in specimens 46, 98, and 342. Small depository
301 surfaces are also identified in the anterior part of the submandibular fossa in specimens 46,

302      92, 98, and 342. A large field of bone resorption activity is observed in the anterior area of

303      this fossa at the level premolar level in specimen 46, whereas small fields are identified in the

304      first molar level in 144 and 342 and in the area extending from the symphyseal region to the

305      ramus in specimen 98.

306      The adult mandibular ramus shows bone resorption surfaces in the buccal side of

307      specimens 46, 52, 92, and 144, whereas specimens 98 and 342 are characterized by depository

308      surfaces. On the one hand, resorbing activity is identified in the coronoid area in specimens

309      46, 92, 98, 144 and 52, in the condyle neck in 46, 92, 98, and 52, along the area running

310      parallel to the posterior border in 46, 92, 52 and 342, in the angle of the ramus in 144 and 52,

311      and close to the inferior border in46, 98, 144, and 52. On the other hand, depository surfaces

312      are observed in the coronoid area in specimens 98 and 342, in the mandibular notch area in92,

313      98, and 342, in the condylar neck in98, 52, and 342, along the area running parallel to the

314      posterior border in specimen98, and in the gonial region of specimen 342. The lingual side of

315      the adult ramus displays predominantly bone formation activity. Bone resorption activity is

316      located in the area between the anterior border and the endocoronoid crest in all specimens, in

317      the neck of the condyle of specimens 46, 92 and 98, in the area parallel to the posterior border

318      of specimens46, 92, 98, and 144, and small resorptive fields in the mandibular notch area in

319      46, 92, 52, and 342. All specimens also display resorbing surfaces in the area associated to the

320      pterigoideus internus and in the corpus-ramus contact area.

321

322      The generalized bone modelling patterns for subadult and adult groups (Figure 4) are

323      obtained through the identification of intraspecific similarities in the bone modelling field

324      distribution of each anatomical region from the facial skeleton and mandible (Enlow and

325      Hans, 1996; Bromage, 1989; Rosas and Martinez-Maza, 2010; Martinez-Maza et al., 2011).

326      The subadult face generalized pattern shows bone formation fields in the upper (glabella and

327    superciliar arch) and middle face (nasal bones and frontal apophysis of the maxillary bone),

328    whereas bone resorption fields extends throughout the lower face (maxillar bone) and the

329    frontal process of the zygomatic bone. In the subadult mandible, the buccal side is

330    characterized by depository surfaces but resorption fields are identified in the alveolar

331    component of the symphyseal region, the coronoid region and the condyle neck. In the lingual

332    side, the anterior region of the mandible and the mandibular notch area are depository

333    whereas the molar region in the submandibular and the sublingual fossae is resorptive.

334        In adults, the generalized pattern of the facial skeleton is predominantly depository but

335    bone resorption activity, comparing with subadult pattern, is reduced to small fields in the

336    glabella, in the frontal apophysis of the maxillary bone and in the frontal apophysis of the

337    zygomatic bone (orbital margin). The resorbing activity of the lower face extends from the

338    canine fossa and along the inferior border of the zygomatic bone. The adult mandible shows

339    in the buccal side resorption activity in the alveolar component of the symphyseal region,

340    along the inferior region of the corpus, and a large field in the corpus-ramus contact area that

341    extends from the inferior margin to the coronoid region. The condylar neck and the

342    mandibular angle region show small resorptive fields. Unlike subadult specimens, the lingual

343    side is characterized by bone formation surfaces. The symphyseal region shows small

344    resorptive fields in the digastric fossa and mental spine region. In the lingual mandibular

345    corpus, the resorption activity is located in the molar region of the submandibular fossa and

346    extends by the coronoid region. A large resorptive field is identified in the gonial region and

347    close to the condyle neck.

348

349    **DISCUSSION**

350        In the present study, we have examined the postnatal growth dynamics of the human

351    facial skeleton and mandible through the analysis of the bone growth modeling activity. The

352    bone modeling patterns from subadult and adult specimens show differences in the

353    distribution of growth fields that demonstrate postnatal changes in bone growth dynamics.

354    Integration of the modelling data from the different anatomical elements informs us about the

355    general growth dynamics of the whole skull and its relationships with ontogenetic postnatal

356    changes of the craniofacial system.

357

358    **Bone growth dynamics in the subadult face and mandible**

359         The modelling pattern of the face and the mandible from the subadult specimens

360    established here is similar to the pattern described by Enlow (1982). On the one hand, the

361    facial skeleton is characterized by depository surfaces in the upper (supraorbital region) and

362    middle face (orbital and nasal regions) and bone resorption fields in the lower face

363    (nasomaxillary region). According to this map, the upper and the middle face grow in a lateral

364    and forward direction, whereas the zygomatic region grows laterally and is relocated

365    posteriorly in agreement with the resorbing surfaces present at the orbital margins. The lower

366    face shows complex growth dynamics related with the preservation of a functional nasal

367    cavity. As reported by Enlow (1982), resorption in the nasomaxillary region occurs

368    simultaneously to bone formation in the posterior region of the face (specifically in the

369    craniofacial sutures) and in the nasal cavity floor and palate. Consequently, the lower face

370    results in a downward or vertical growth of the maxilla, the formation of the *canine fossa,* a

371    depression on the external surface of the maxillary bone, and the increase in height of the

372    nasal cavity (Kurihara et al., 1980; Enlow and Hans, 1996; McCollum and Ward, 1997).

373

374         On the other hand, the mandible pattern is characterized by depository surfaces in the

375    symphyseal region and the anterior corpus, whereas the posterior region of the corpus and the

376    ramus show complex modelling patterns. According to these data, the mandible shows a

377  forward growth associated to the deposition in the symphysis and the corpus, as well as to the

378  lengthening of the posterior region of the corpus. At the same time, the ramus and the molar

379  region of the corpus show a main lateral growth, whereas the condyle and coronoid regions

380  show a forward growth with a posterior relocation of the ramus. Interestingly, the lingual side

381  of the corpus shows an opposite pattern to that proposed by Enlow (1982) –resorption in the

382  sublingual fossa and the region anterior to the mandibular foramen, and formation in the

383  submandibular fossa– suggesting a marked lateral growth of the molar region in the

384  mandibular corpus and ramus. Other differences regarding the extension of the resorbing

385  surfaces in the buccal side of the ramus could be considered artefacts due to the variability of

386  the distribution of modelling fields observed in the human mandible (Enlow and Harris, 1964;

387  Kurihara et al., 1980; Hans et al., 1995). It is also worth mentioning that the symphyseal

388  region presents a human-specific resorption field in the alveolar component of the buccal side

389  related to the dental movements and the mental growth, and being involved in the

390  development of the human chin (Enlow and Hans, 1996).

391       Variability in the distribution of the modelling fields is mainly observed at the anterior

392  lower face and at the mandibular ramus. Differences in the distribution and the extension of

393  the resorption fields of the anterior face agrees with the modelling data provided by Kurihara

394  et al. (1980) for humans up to 14 years old, but disagrees with the mainly-depository anterior

395  lower face observed by McCollum (2008). As annotated by Kurihara et al. (1980) and later by

396  McCollum (2008), variability in the modelling maps from this facial region could be due to

397  morphological variations associated to differences in geographic origin. Variability in the

398  mandible ramus involves the extension and the location of the resorption fields in the

399  coronoid and the condyle neck, due to lateral adjustments while growing upward and

400  relocating posteriorly. Besides these two main areas, variability is also observed in the buccal

401  symphyseal region -previously reported by Kurihara et al (1980)- and in the mandibular

402    corpus -opposite to the general pattern established here, individual 126 submandibular fossa

403    pattern resembles to that established by Enlow and Hans (1996)-.

404

405    **Bone growth dynamics in the adult face and mandible**

406    We have established for the first time, to our knowledge, the bone modelling pattern of

407    the face and the mandible from adult humans. The facial pattern is mainly depository with

408    resorption surfaces restricted to the nasal region, the canine fossae, and the inferior margin of

409    the zygomatic region. General growth directions from this pattern indicate a lateral,

410    downward and forward growth of the whole adult face. Like in subadult specimens, the

411    nasomaxillary region shows complex growth dynamics associated to the functional spaces

412    such as the nasal and the oral cavities (Moss, 197x). Bone resorption in the nasal region could

413    be associated with the increase in high of the nasal aperture (CITA) and the forward

414    projection of this region (CITA). Although there is no data about the nasal floor and palate for

415    adult specimens, the modelling map obtained in our study and the morphometric data

416    obtained in previous works (CITAS) allow us to hypothesize that the lower face shows a

417    downward and forward growth of the maxilla associated to the increase of the nasal cavity.

418    Resorbing surfaces in the anterior nasomaxillary region of the adult face are restricted to the

419    area of the canine fossae, likely related to its development.

420    In the adult mandible, the symphysis and the anterior region of the corpus are mainly

421    depository with resorbing surfaces restricted to the alveolar component of the buccal side of

422    the symphysis, resembling the pattern of subadult specimens. Slight differences are found in

423    the lingual side of the symphysis which show resorption fields in sites associated to muscle

424    attachment (gastricus, genioglossus, geniohyoideus and the anterior part of the mylohyoideus

425    muscles). The pattern of the posterior region of the corpus and the ramus highly differs from

426    the subadult patterns established in the present and previous works (Enlow and Hans, 1996;

427  Kurihara et al., 1980). In the adults, resorption extends to cover, in the buccal side, the

428  posterior region of the *corpus* and the anterior region of the *ramus*, and, in the lingual side,

429  the submandibular fossa of the *corpus*, and the coronoid region and the lower half (gonial

430  area) of the *ramus*. This map indicates a forward growth direction of the symphysis and a

431  lateral growth of the molar region of the *corpus*, whereas the anterior region of the *ramus*

432  grows in a posterior and medial direction. The posterior region of the *ramus* experiments

433  complex growth dynamics characterized by a lateral growth of the gonial area, a medial

434  growth of the mandibular notch area, and a lateral and medial growth of the condyle area.

435  These growth directions indicate that the lower part of the *ramus* is taking a vertical position

436  while the upper area increases in width and grows backwards.

437      The modelling pattern of the facial skeleton and the mandible varies less in adult than

438  in subadult specimens. Variability is observed in the extension of the resorption fields of the

439  anterior nasomaxillary region and the mandibular *ramus*, as observed in subadults. As

440  proposed by Kurihara et al. (1980) and McCollum (2008) for subadult specimens, we

441  hypothesize that these variations could respond to individual differences in functional or

442  morphological characteristics (Kurihara et al., 1980; Enlow and Hans, 1996).

443

444  **Postnatal changes in the growth dynamics of the human face**

445      According to the data obtained in the present study, the facial skeleton and mandible

446  from both subadult and adult specimens show a general downward and forward growth, in

447  agreement with Enlow and Hans (1996). However, bone modelling patterns differ among both

448  age groups, showing a marked spatial gradient, from a anterior region of the maxilla where

449  most changes concentrate to the almost constant facial regions in the proximity of the

450  neurocranium. Interpretation of these ontogenetic changes would benefit from an integrative

451  perspective taking into consideration how the different skeletal components within the

452 craniofacial system interact to maintain the functional and structural balance whereas they

453 increase in size during the postnatal development (Enlow and Hans, 1996; Moss and Young,

454 1960; Moss, 1962).

455      During the subadult stage, the facial skeleton experiences a downward growth and a

456 forward displacement, together with the lengthening of the maxilla. This growth and

457 displacement of the facial block is accompanied by an upward maxillary rotation

458 (airorhynchy) due to the higher bone growth in the craniofacial sutures that attach the midface

459 to the basicranium than in the anterior region of the maxilla (Björk and Skieller, 1976;

460 Bromage, 1989; McCollum and Ward, 1997). This rotation of the premaxilla would be

461 countered by a downward rotation through compensatory resorption activity in the external

462 surfaces of the anterior region of the maxilla (Björk, 1968; Björk and Skieller, 1976; 1983;

463 see also Bromage, 1989; McCollum and Ward, 1997 and references there in). The resulting

464 downward facial growth vector contributes to the relative orthognathy in humans (Bromage,

465 1989). Simultaneously, the whole mandible is displaced forward and downward to

466 compensate the displacements of the maxilla and to maintain the occlusal plane (Moss, 197x;

467 Enlow and Hans, 1996). The forward displacement of the face becomes balanced through the

468 growth of the posterior region of the mandibular corpus, whereas the vertical growth is

469 compensated by the increase in height of the *ramus* and, particularly, the condyle (Enlow and

470 Hans, 1996). During this displacement, the mandibular *corpus* increases in width at the

471 anterior region, whereas the molar region and the *ramus* show a lateral drift. The lateral drift

472 and the vertical growth of the *ramus* have been related to the growth of the basicranium as a

473 way to keep the mandible in contact with the neurocranium through the temporomandibular

474 joint.

475      With adulthood, the modelling pattern changes reflecting the biological changes that

476 take place with maturation. Most important changes occur in the anterior region of the face,

477 where the resorbing surfaces that occupy most of the immature nasomaxillary region become

478 restricted to the canine fossae whereas formation occupy the remaining surface. This

479 modelling pattern would indicate a direct forward growth of the nasomaxillary complex

480 during adulthood opposite to the primary displacement that takes place in immatures.

481 Modelling changes run parallel to the fusion of the craniofacial sutures and the end of the

482 brain growth that occur around 18 to 20 years after birth (Madeline and Elster, 1995; Björk,

483 2007). Considering that the posterior growth of the face in immature individuals occur by

484 bone formation at the craniofacial sutures (Enlow and Hans, 1996), the fusion of these sutures

485 and the subsequent arrest of the bone growth in the area would limit the growth of this

486 posterior region of the facial skeleton. Thus, the modelling pattern and the biological

487 constraints indicate that the facial growth in the adult stage is restricted to the anterior region

488 and suggest a forward growth of the whole facial skeleton with an increase in the height of the

489 nasal region.

490 The mandible also responds to these developmental changes, as reflected in its

491 modelling pattern. Ontogenetic changes concentrate in the *ramus*, a region that increases in

492 height at a rate similar to the nasomaxillary region, resulting in a increase of the nasal cavity

493 while it maintains the occlusal plane. The *ramus* also grows laterally and medially to keep the

494 vertical position and the contact with the neurocranium through the temporomandibular joint

495 (Enlow and Hans, 1996). As the neurocranium and basicranium stops growing in the adult

496 stage, the distance between the mandible fossae becomes established and the condyles would

497 adapt to this distance changing the growth of the condyles and maintaining a functional

498 position.

499 Changes in the modelling pattern of the face and the mandible during adulthood have

500 been related to the necessity of increasing the volume of the oral and nasal cavities to cope the

501 physiological requirements of the organism. It has been suggested that growth and

502    development of the craniofacial complex is related to the nasal respiratory function (Hall,

503    2005; Chinn *et al.,* 2006; Weinstein, 2008;   Gungora and Turkkahramanb, 2009). The

504    coordinated development of the respiratory system and body size is likely a factor that could

505    influence the facial growth particularly for the nasomaxillary complex and the mandible (see

506    Bastir, 2008 and references therein). In adittion, the craniofacial growth is also related to size,

507    shape, and energetics of the entire body (Bastir, 2008). In this line, the forward growth of the

508    anterior face that occurs during the adulthood would reflect that the neurocranium has stop

509    growing but the body still grows together with all its physiological requirements.

510         In conclusion, our results demonstrate postnatal changes in the growth dynamics of the

511    facial skeleton and the mandible. We hypothesize that these changes are related to biological

512    events occurred in the craniofacial system such as the fusion of the craniofacial sutures, or the

513    reaching of the adult size of the brain and the neurocranium. Thus, in the adults, a new

514    relationship among skeletal elements of the skull emerges but the face needs to continue

515    growing, increasing the nasal and oral cavities in order to maintain a functional and structural

516    balance.

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694

695    **TABLE**

696    **Table 1.** List of the *Homo sapiens* specimens from the Anthropological Collection of the

697    University of Coimbra (Portugal) analysed with Reflected Light Microscopy.

| Specimen | Age (years old) | Age group | Sex |
|----------|-----------------|-----------|--------|
| 101 | 12 | Subadult | Female |
| 218 | 10 | Subadult | Female |
| 284 | 17 | Subadult | Female |
| 100 | 7 | Subadult | Male |
| 100A | 11 | Subadult | Male |
| 126 | 8 | Subadult | Male |
| 52 | 38 | Adult | Female |
| 144 | 29 | Adult | Female |
| 342 | 28 | Adult | Female |
| 46 | 38 | Adult | Male |
| 92 | 27 | Adult | Male |
| 98 | 24 | Adult | Male |

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**FIGURE LEGENDS**

714 **Figure 1.** Bone formation (left) and resorption (right) surfaces identified in the sample of

715 *Homo sapiens* analysed in this study. Image on left shows a bone formation surface from the

716 buccal side of the mandibular corpus region (specimen 126), which is characterized by

717 collagen fiber bundles. Image on right shows a bone resorption surface from the maxilla

718 (specimen 218) characterized by Howship's lacunae. Scale bar: 100 µm.

719

720 **Figure 2.** Schematic bone modeling patterns from the specimens of the subadult group. Black

721 colour: bone formation surfaces; grey colour: bone resorption surfaces.

722

723 **Figure 3.** Schematic bone modeling patterns from the specimens of the adult group. Black

724 colour: bone formation surfaces; grey colour: bone resorption surfaces.

725

726 **Figure 4.** Generalized bone modeling patterns from subadult and adult humans. Stippling

727 areas represent bone deposition and grey areas represent bone resorption. Black arrows show

728 the direction of growth by bone formation and white arrows the direction of growth by bone

729 resorption.

730

731 **Figure 5.** Figure shows the growth vectors inferred from the generalized bone modeling

732 patterns from subadult and adult humans. Black arrows show the direction of growth by bone

733 formation and white arrows the direction of growth by bone resorption.