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Several infra-cranial non-metric variations in a single Neolithic individual: A common genetic underlying predisposition?

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Review

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3 **Several infra-cranial non-metric variations in a single Neolithic individual: A common**
4 **genetic underlying predisposition?**
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43 **Running title:** Several infra-cranial non-metric variations in a Neolithic individual
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46 **Keywords**

47 Non-metric variation, genetic etiology, mechanical stress, Neolithic
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51 **Abstract**

52 Non-metric variations have been the subject of anatomical and anthropological studies for
53 more than a century. In this study, we present an individual from Sion (Canton of Valais,
54 Southern Switzerland) dated from the Middle Neolithic who shows evidence for four non-
55 metric variations. This young adult male presents an *os acromiale*, spondylolysis, a bipartite
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3 patella and bilateral *calcaneus secundarius*. These non-metric variations have a low frequency
4 in most populations (less than 10%) and for each of them the origin is usually considered to
5 be genetic, environmental, or a combination of both. This case is of interest for understanding
6 the potential genetic origin of these non-metric variations as well as for demonstrating their
7 usefulness in bioarcheological analysis.
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11 12 13 INTRODUCTION

14 Non-metric variations, also called discrete traits, have been the subject of anatomical and
15 anthropological studies for more than a century. These minor non-pathological skeletal
16 variants can be found throughout the human skeleton (Gemmerich Pfister, 1999).
17

18 Non-metric variations are commonly used as a measure of biological or genetic distance and
19 variation in archaeological human skeletal samples (e.g. Berry, 1974; Crubézy et al., 1999),
20 although some of them are also considered as activity-related skeletal morphologies (e.g.
21 Stirland, 1987; Villotte et al., 2014). The developmental genetic bases for most of these
22 discrete morphological variants are not well known (Hauser and De Stefano, 1989). A few
23 traits have been studied in humans (Saunders and Popovich, 1978), but most of what is known
24 comes from studies of other primates (for a review see: Wilmore et al., 2012) or mice
25 (Grüneberg, 1952). Genetic, epigenetic (cellular and physiological traits inherited by daughter
26 cells and not caused by changes in the DNA sequence), and environmental factors are
27 probably involved in the appearance of non-metric variations, so a polyfactorial origin could
28 be posited for the appearance of most non-metric variations (Konigsberg, 1993).
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38 In this study, we present a single individual in whom four infra-cranial non-metric variations
39 were observed.
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43 MATERIAL AND METHOD

44 The individual presented here come from a necropolis of 25 burials (24 single inhumations
45 and one double burial), discovered in 1988 and excavated by Brunier in Sion, at the so-called
46 chemin des Collines (Canton of Valais, Southern Switzerland) (Moinat et al., 2007).
47 Radiocarbon determinations indicate a date for the necropolis of between 4550 and 4100 BC,
48 which corresponds to the Middle Neolithic (Moinat et al., 2007).
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53 The non-metric variations were observed and scored as present/absent. The sex of this
54 individual was determined using two methods applied to the *ossa coxae* (Bruzek, 2002;
55 Murail et al., 2005). Age at death was estimated using the stage of epiphyseal fusion of the
56 bones (Scheuer et al., 2000).
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RESULTS

The individual is an adult male, around 16-21 years old. The skeleton is in a moderately well-preserved state. The cranium and mandible and most of the infra-cranial bones are incomplete or fragmentary. Some of the long bones and the left *os coxae* are complete.

Lumbar vertebrae are poorly preserved but L4 and L5 were identified. L5 presents a spondylolysis (a separation at the *pars interarticularis* of the neural arch) on the right side (figures 1a, b). The left side is absent. The surface at the separation is smooth and looks like a fibrocartilaginous enthesis (see Boszczyk et al., 2006). L4 does not present any trace of spondylolysis on the right side and the left side is missing. We also observed two inferior articular processes, one right and one left, which presented spondylolysis. The right process corresponds with the body of L5 but it was impossible to associate the left one to the body and the two processes have very different shapes. Thus, this individual presents either: a case of bilateral spondylolysis of L5 with asymmetry of articular processes, unilateral cases of spondylolysis of L4 and L5, or a bilateral spondylolysis of L5 and unilateral spondylolysis of L4.

The individual has an *os acromiale* on the right scapula (figures 1c, d). Considering the age of the individual it is possible to confuse *os acromiale* with a normal, unfused acromial epiphysis. However, according to the classifications of Sammarco (2000) and Case et al. (2006), it looks clearly to be an *os acromiale* with a free, separate fragment and a well-defined articulation: it does not have the appearance of an epiphysis, there is pitting present, and the joint is linear and horizontal to the axis of the acromion. The left scapula is absent.

The individual shows a bipartite right patella (figures 2a, b), the left bone being absent. Only the body of the right patella is present, the bipartite fragment is missing. There is an oblique rupture at the junction between the medial part and the lateral part of the body.

A *calcaneus secundarius* (a small accessory bone located on the anterior facet of the calcaneus) is present on both calcanei (figures 2c, d), and it is identified via the presence of a notch on the anterior facet.

The four infra-cranial non-metric variations seen in this individual are seen in low frequencies in most contemporary and archaeological populations (table 1). Such a case with several non-metric variations, each presenting a low frequency is very rare (Saunders, 1978). A study of two French collections shows very few cases and the association of those four traits was not found in any of 295 adult skeletons analysed (table 2) (Verna, 2014). Frequencies for three of

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3 these non-metric variations¹ are provided in the table 3 for the Middle Neolithic from
4 Southern Switzerland. None of these variations is especially frequent in this prehistoric
5 sample, and a combination of all of them was not seen apart from the individual presented
6 here.
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10 Apart from these non-metric variations, the skeleton displays only a few other notable
11 features: a metopic suture, shovelling of the upper central incisors, diminutive upper lateral
12 incisors, lateral squatting facets on both tibiae, and a new bone formation on the posterior
13 surface of the left tibia, in the area of the *M. soleus* attachment site.
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17 18 **DISCUSSION AND CONCLUSIONS**

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20 Mann (1990) examined 1,367 calcanei from several populations. According to him, the origin
21 of *calcaneus secundarius* is congenital or the result of traumatic injury of the immature
22 calcaneus (i.e. at a cartilaginous stage) resulting in a “pinched off” island of cartilage and an
23 accessory center of ossification. Anderson (1988) suggested that *calcaneus secundarius* was
24 the consequence of a congenital defect of ossification with mechanical factors causing the
25 separation of the ossicle. An association of *calcaneus secundarius*, *os tibiale externum*, and *os*
26 *vesalium*, has been reported in one individual in a clinical and radiographic study (Heikel,
27 1962).
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33 Genetic predisposition has been reported by several authors for the appearance of
34 spondylolysis (Haukipuro et al. 1978; Wynnedavies and Scott 1979), but at the same time the
35 prevalence of spondylolysis seems to be higher in the young athletic population (adolescent
36 and young adult) than in the general population, 15% for gymnasts for example (Jackson et
37 al., 1976; Goldstein et al., 1991; Soler and Calderon, 2000). Moreover Boszczyk et al. (2006)
38 found that the lysis-zone tissue had an ordered collagenous structure with distinct
39 fibrocartilaginous entheses at both ends, suggesting that compressive and shear forces act at
40 this area.
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46 Stirland (1987) supports a mechanical origin by which the *os acromiale* results from
47 mechanical strain on the developing acromion, whereas the genetic origin is supported by
48 others (Angel et al., 1987; Sammarco, 2000; Hunt and Bullen, 2007). According to Case et al.
49 (2006) the most likely explanation is a combination of genetic predisposition and high
50 mechanical stresses.
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55 While the cause of a painful bipartite patella is relatively well understood (e.g. Gaheer et al.,
56 2009; Oohashi, 2015), the origin of this variation is not. The patella ossifies from one center
57 in most children, but in ca. 25% of the population two or three centers are present (Gaheer et
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3 al., 2009). While this is considered as a normal variant by many authors, some others consider
4 the accessory ossification centre(s) as the result of a disorder of ossification in the primarily
5 cartilaginous formation of the patella due to abnormal stresses produced by excessive action
6 of the inserting musculature during growth (Soren and Waugh, 1994). The ossicle may fuse to
7 the main patellar body (see for instance Anderson, 2002 for an archeological case) or stays
8 unfused. Why the fusion occurs or does not is still not understood (e.g. Soren and Waugh,
9 1994; Anderson, 2002), but it is likely that genetic predisposition plays a role in some cases
10 (Aloisio, 1961). It is also noteworthy that a case of bipartite patella has been described in
11 association with an autosomal dominant disorder called nail-patella syndrome (Kumar et al.,
12 1999).

13
14 Thus, for all these infra-cranial non-metric variations, high mechanical stresses during
15 growth, a genetic predisposition, or a combination of both are evoked to explain their origin.
16 For all of these anatomical areas, authors indicate that fractures due to acute trauma can occur
17 during adulthood, but: 1) they are very uncommon, and 2) usually they can be easily
18 distinguished from the non-union form (e.g. Heikel, 1962; Merbs, 1996; Anderson, 2002;
19 Case et al., 2006). The changes seen in the individual studied here present the "classical"
20 aspect of a non-union, and so do not seem related to acute trauma.

21
22 It is possible that this individual performed a range of strenuous physical activities during
23 childhood or adolescence leading to the changes described here. However, even in that case,
24 considering the fact that the four non-metric traits are very similar in their expression (an
25 unattached piece of bone), it seems very likely that this individual was genetically
26 predisposed. Our first conclusion is that in some cases at least, the presence of one of these
27 traits in a single individual or in a sample may be more related to genetic conditions than to
28 mechanical stresses, and thus authors must be cautious before considering these traits in
29 studies of activity-related skeletal morphology. Our second conclusion concerns the
30 relationship between these traits. Indeed, the unique combination of these four non-metric
31 variations, being rare and very similar in their expression, may indicate that a common DNA
32 coding area is involved in their presence.

33
34 The systematic research for combinations of these infra-cranial non-metric variations, along
35 with descriptions of other non-metric characteristics that can be associated with a "syndrome"
36 (in the present case possibly the metopic suture, and the diminutive upper lateral incisors)
37 may lead to a better understanding of the underlying genetic control of the expression of these
38 morphological changes in the skeleton.

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The authors declare no conflict of interest.

Footnotes

Presence or absence of *calcaneus secundarius* was not recorded systematically at the time of the original study on activity-related skeletal morphological changes. So, even if no other case was apparently present, frequencies cannot be calculated.

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3 Legend of figures
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5 **Figure 1:** A. Spondylolysis of the fifth lumbar vertebra. B. Articular process of lumbar
6 verterba with spondylolysis. C. *Os acromiale* on the right scapula. Acromion from the
7 postero-superior view. D. Part of the acromion process with the line indicative of non-fusion.
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9 **Figure 2:** A. Bipartite right patella. Anterior view. B. Bipartite right patella. Posterior view.
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11 C. *Calcaneus secundarius* on the right calcaneus. Dorsal view. D. *Calcaneus secundarius* on
12 the right calcaneus. Plantar view.
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For Peer Review

Table 1: Frequencies of the four non-metric variations in various current and archaeological populations

Non-metric variations	%	Liaison with sex	Liaison with laterality	References
OA	0.7 - 20	M > F, North American	U>B, L>R	Saunders, 1978; Sammarco, 2000; Case et al., 2005; Hunt and Bullen, 2007; Kumar et al., 2013; Verna, 2014
S	3.2 - 33	M > F	B>U	Stewart, 1953; Saunders, 1978; Merbs, 1989; Merbs, 1996; Masnicova and Benus, 2003; Verna, 2014
BP	1.4 – 8.5	M > F	-	Saunders, 1978; Lawson, 1994; Anderson, 2002; Verna, 2014
CS	1.4 – 14.3	M > F, European	U>B	Anderson, 1988; Mann, 1990; Verna, 2014

OA = *os acromiale*, S = spondylolysis, BP = bipartite patella, CS = *calcaneus secundarius*. M = male, F = female, U = unilaterally, B = bilaterally, L = left, R = right.

Table 2: Frequencies and association of the four non-metric variations in two French collections (one contemporary and one from Middle Ages)

Non-metric variations	Olivier		Saint Jean de Todon	
	n/N	%	n/N	%
OA	5/91	5.5	15/136	11.0
S	5/85	5.9	8/167	4.8
BP	7/82	8.5	1/129	0.8
CS	6/63	9.5	16/121	13.2
OA + S	0/63	0	1/121	0.8
S + BP	0/63	0	0/121	0
BP + CS	1/63	1.6	0/121	0
S + CS	0/63	0	1/121	0.8
OA + CS	0/63	0	3/121	2.5
OA + BP	0/63	0	0/121	0
OA + S + BP	0/63	0	0/121	0
S + BP + CS	0/63	0	0/121	0
OA + BP + CS	0/63	0	0/121	0
CS + S + OA	0/63	0	0/121	0
OA + S + BP + CS	0/63	0	0/121	0

n: number of cases, N: number of individuals for which the present or absence of a trait or of an association can be scored. OA = *os acromiale*, S = spondylolysis, BP = bipartite patella, CS = *calcaneus secundarius*

Table 3: Frequencies of non-metric variations and associations in the Middle Neolithic sample for Switzerland (73 individuals from Barmaz I, Barmaz II, Chamblandes, Sion Collines, Sion Ritz, Sion St Guerin, St Leonard 4, Corseaux).

Non-metric variations	n/N	%
OA	2/44	4.5
S	4/51	7.8
BP	2/54	3.7
OA + BP	1/32	3.1
OA + S	1/34	2.9
S + BP	1/38	2.6
OA + BP + S	1/28	3.6

n: number of cases, N: number of individuals for which the present or absence of a trait or of an association can be scored. OA = *os acromiale*, S = spondylolysis, BP = bipartite patella.



A. Spondylolysis of the fifth lumbar vertebra. B. Articular process of lumbar vertebra with spondylolysis. C. Os acromiale on the right scapula. Acromion from the postero-superior view. D. Part of the acromion process with the line indicative of non-fusion.
119x80mm (300 x 300 DPI)

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A. Bipartite right patella. Anterior view. B. Bipartite right patella. Posterior view. C. Calcaneus secundarius on the right calcaneus. Dorsal view. D. Calcaneus secundarius on the right calcaneus. Plantar view. 80x99mm (300 x 300 DPI)