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Short Communication

Absence of the *-116A* variant of the butyrylcholinesterase *BCHE* gene in Guarani Amerindians from Mato Grosso do Sul

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Abstract

Butyrylcholinesterase (BChE; EC 3.1.1.8; Online Mendelian Inheritance in Man (OMIM) number 177400) is an enzyme found in many human tissues and encoded by the *BCHE* gene, of which 65 variants have been identified. In a recent study we found that the *-116A* variant of exon 1 of the *BCHE* gene was associated with lower mean BChE activity. The present study analyzed the -116 single nucleotide polymorphism (SNP) in 253 Guarani Amerindian Brazilians from the state of Mato Grosso do Sul (148 Guarani-Kaiowá, 83 Guarani-Ñandeva and 22 Kaiowá-Ñandeva descendants) and verified that they were all homozygotic for the *-116G* variant. A comparative analysis of the -116 site in nine vertebrate species indicated the *-116A* variant as the ancestral type. This is the first study of the -116 SNP in Amerindians and it is therefore difficult to infer whether or not the *-116A* variant was always absent from southern paleo-Amerindians or was present and then subsequently lost due to evolutionary factors.

Key words: Amerindians, *BCHE* gene, Guarani-Kaiowá, Guarani-Ñandeva.

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Human butyrylcholinesterase (BChE (EC 3.1.1.8), Online Mendelian Inheritance in Man (OMIM) number 177400) is an enzyme synthesized in liver and found in many tissues (Kutty, 1980) and which hydrolyses choline aliphatic esters such as butyrylcholine and some muscle relaxants (succinylcholine, mivacurium), and non choline esters such as salicylic acid, cocaine and the local anesthetic procaine (Lockridge, 1992). Genetic variants of BChE have been associated with body mass index and height (Souza *et al.*, 2005a) and expression of this enzyme has also been related to cell proliferation during embryonic development (Layer, 1983). Human butyrylcholinesterase is encoded by the *BCHE* gene (3q26.1-q26.2), of which 65 variants have already been described (Souza *et al.*, 2005b).

The distribution of *BCHE* gene variants has been investigated at the DNA level by Souza *et al.* (1998) in two sample groups from Southern Brazil, one containing Brazilians of mainly European descent and the other containing Brazilians of mixed African and European descent, and by Furtado *et al.* (2006) in Amerindian Brazilians, with the aim of contributing to a better understanding of both the evolution of the *BCHE* gene and of Brazilian population groups. Furtado *et al.* (2006) investigated the *BCHE* gene variability in Guarani Amerindian Brazilians from the Kaiowá and Ñandeva groups from the Brazilian state of Mato Grosso do Sul. In 244 of these Amerindians, the *1615A* variant of exon 4 (single nucleotide polymorphism – SNP, G/A: rs1803274; *K* variant; *p.A539T*) occurred with a frequency of 3.7% ± 0.9%, significantly lower than that found in Brazilians of European descent (18.4% ± 2.8%; Souza *et al.*, 1998). The mean BChE activity was examined for 86 of these Amerindians and was found to be 4.01 ± 0.15 KU/L (Furtado *et al.*, 2006), significantly lower than that for Brazilians of European descent but significantly higher than that for individuals from the Pacaás Novos, Sateré Mawé and Tenharim Brazilian Amerindian groups. Although the *1615A* variant had previously been associated with lower BChE activity due to the decreased number of molecules (Rubinstein *et al.*, 1978), Altamirano *et al.* (2000) showed that the K and wild-type enzymes presented similar activity, protein turnover and tetramer formation. Furtado (2005) investigated a group of Brazilian blood donors of European descent from the southern Brazilian city of Curitiba and showed that the decreased BChE activity associated with the K enzyme only occurs in the presence of the *-116A* mutation of exon 1 (SNP: G/A; rs1126680), which is in a transcribed but untranslated region. In this blood donor sample, the *-116A* allele frequency was 8.5% ± 1.5% and linkage disequilibrium

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analysis estimated that 94% of haplotypes with *-116A* also presented the *1615A* variant (D' = 91.2%).

We used -116 SNP (G/A) genotyping by polymerase chain reaction and single strand conformation analysis (PCR-SSCA) following the methodology of Furtado (2005) to investigate the occurrence of the *BCHE* gene *-116A* allele in 253 Amerindian Brazilians, consisting of 148 Guarani Kaiowá, 83 Guarani Nãndeva and 22 Kaiowá-Ñandeva descendent Amerindians from a region (20°24' S, 54°58' W to 23°93' S, 56°55' W) in the Brazilian state of Mato Grosso do Sul.

The result showed that all the 253 examined Amerindians were homozygous for the *-116G* allele. Although this Amerindian group had 18 individuals with the *1615A* variant (16 heterozygotes and 2 homozygotes), the *-116A* variant was not found.

This is the first genotyping of the -116 (G/A) SNP of the *BCHE* gene in Amerindians. Data from the HapMap (ref SNP rs10513620) on 60 Utah residents of northern and western European descent, 45 Han Chinese (Beijing, China), 44 Japanese (Tokyo, Japan) and 60 Yoruba (Ibadan, Nigeria) showed the presence of the *-116A* allele only in Utah residents with a 5.8% frequency.

Considering that no information for other Amerindian samples has been reported for this SNP and that small samples were examined for groups with non-European ancestry, it is difficult to infer whether paleo-Amerindians had the *-116A* mutation and subsequently lost it due to micro evolutionary processes or if this mutation was not present in the founder group. Nunes (2007) determined that the *-116A* mutation was the ancestral mutation for this site in vertebrates based on the fact that this was the wild-type mutation present in the domestic dog *Canis familiaris* (GeneBank XM 545267), the domestic cat *Felis catus* (NM 001009364), the tiger *Panthera tigris* (AF 053484), the rhesus monkey *Macaca mulatta* (XR 011736) and the common chimpanzee *Pan troglodytes* (XM 516857) while in the brown rat *Rattus norvegicus* (NM 022942) and the house mouse *Mus musculus* (NM 009738) the wild type was the *-116C* variant and in the chicken *Gallus gallus* (AJ 306928) it was the *-116G* variant, similar to the most frequent variant in *Homo sapiens* (NM 000055). The fact that three other Brazilian Amerindian groups (Pacaás Novos, Sateré Mawé and Tenharim) showed lower BChE activity than this Guarani sample, together with data on the association of the *-116A* variant with low BChE activity, make these three groups important for the investigation of this variant.

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