



The association between earlobe crease (Frank's sign) and cognitive performance is related to age. Results from the Atahualpa Project



Oscar H. Del Brutto^{a,*}, Robertino M. Mera^b, Mauricio Zambrano^c, Aldo F. Costa^a

^a School of Medicine, Universidad Espíritu Santo – Ecuador, Guayaquil, Ecuador

^b Vanderbilt University Medical Center, Nashville, TN, USA

^c Community Center, The Atahualpa Project, Atahualpa, Ecuador

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ABSTRACT

Background: Earlobe crease (ELC) has been linked to cardiovascular diseases, but information on its association with cognitive decline is limited. We aimed to assess the association between ELC and cognitive performance in community-dwelling adults living in rural Ecuador.

Methods: Of 863 individuals aged ≥ 40 years enrolled in the Atahualpa Project, 629 (73%) were included. ELC were visually identified by two independent raters, and cognitive performance was measured by the Montreal Cognitive Assessment (MoCA). Using generalized linear and interaction models, adjusted for demographics, cardiovascular risk factors and edentulism, we assessed the association between ELC and cognitive performance, as well as the influence of age in this association.

Results: ELC was present in 246 (39%) individuals, and the mean MoCA score in the entire population was 21.9 ± 4.7 points. A generalized linear model showed no relationship between ELC presence and the MoCA score ($p = 0.449$). In this model, covariates remaining significant were age ($p < 0.001$), physical activity ($p = 0.014$) and edentulism ($p < 0.001$). When participants were stratified according of quartiles of age, the MoCA score did not differ according to the presence or absence of ELC. Weighted exposure-effect models – using ELC and the MoCA score as the exposure and outcome (respectively) – revealed no association between both variables.

Conclusions: The association between ELC and the MoCA score is mainly related to age. These findings might be explained by the high prevalence of ELC and cognitive decline in older adults.

1. Introduction

The earlobe crease (ELC) is a wrinkle extending from the tragus to the outer border of the earlobe (Frank, 1973). The presence of ELC has been associated with coronary artery disease and other cardiovascular events (Christoffersen et al., 2014; Edston, 2006; Nazzal, Hijazi, Khalila, & Blum, 2017; Shmilovich et al., 2012). In addition, the recently reported association between ELC, cognitive decline and neuroimaging signatures of cerebral small vessel disease would suggest a role of this sign in the recognition of subjects at risk for developing vascular cognitive impairment (Lee et al., 2017). That study was conducted in older adults enrolled in dementia studies or attending a memory clinic in Korea, and the predictive value of ELC for the detection of subjects with poor cognitive performance has yet to be confirmed in unbiased population samples. Using the Atahualpa Project cohort, we aimed to assess the relationship between the presence of ELC

and cognitive performance in community-dwelling adults living in rural Ecuador.

2. Methods

2.1. Study population

Atahualpa is a rural village located in coastal Ecuador that achieves several requisites to be considered an optimal setting for the practice of epidemiological studies. More than 95% of the population belongs to the Ecuadorian native/Mestizo ethnic group, and their lifestyle, socio-economic status and dietary habits are homogeneous. These consistencies reduce the risk of unexpected confounders at the time of analyses. Methodology of the Atahualpa Project has been described elsewhere (Del Brutto, Peñaherrera et al., 2014). In brief, all Atahualpa residents aged ≥ 40 years identified during door-to-door surveys were

* Corresponding author at: Air Center 3542, PO Box 522970, Miami, FL 33152-2970, USA.

E-mail address: odelbrutto@uees.edu.ec (O.H. Del Brutto).

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Fig. 1. Earlobe crease in an Atahualpa resident.

invited to participate, and those who signed the informed consent were registered. The I.R.B. of Hospital-Clinica Kennedy, Guayaquil, Ecuador (FWA 00006867) approved the study.

2.2. Earlobe crease identification

Both earlobes were examined with the subject in the sitting position, and an ELC was considered to be present when the individual has a wrinkle extending from the tragus to the outer border of the earlobe (Fig. 1). Subjects with creases related to earrings and those who have physical damage distorting anatomy of the earlobe were excluded. Two investigators, blinded to each other's assessments and to clinical data, independently assessed the earlobes. Kappa coefficients for inter-rater agreement were adequate for ELC presence ($k = 0.95$) and discrepancies were resolved by consensus.

2.3. Cognitive assessment

Cognitive performance was assessed by the use of the Spanish version of the Montreal Cognitive Assessment (MoCA) test (www.mocatest.org,[©] Z. Nasreddine MD, version 07 November 2004). The MoCA evaluates major cognitive domains, including visuospatial-executive

(trail making B task, 3-dimensional cube copy, and clock drawing); naming (unfamiliar animals); language (sentence repetition, and a phonemic fluency task); short-term memory (delayed recall or words); abstraction (verbal abstraction); attention and calculation (digits forward and backward, target detection using tapping, serial 7's subtraction); and orientation (time and space). Maximum MoCA score is 30 points, with an additional point given to persons with ≤ 12 years of education (Nasreddine et al., 2005). We did not use a cutoff score for defining cognitive impairment, but the continuous MoCA score to avoid problems related to poor reliability of specific cutoffs in less-educated populations (Gómez, Zunzunegui, Lord, Alvarado, & García, 2013).

2.4. Clinical covariates investigated

Demographics, cardiovascular risk factors and edentulism were selected as confounding variables. These confounders were assessed through interviews and procedures previously described in the Atahualpa Project (Del Brutto et al., 2013). We used the American Heart Association criteria to assess smoking status, physical activity, diet, the body mass index, blood pressure, fasting glucose, and total cholesterol blood levels (Lloyd-Jones et al., 2010). Severe edentulism was defined in individuals having < 10 remaining teeth (a rural dentist performed a dental examination in all cases). Edentulism was used as a surrogate of chronic inflammatory periodontal disease, and was included as a covariate as it has shown to be related to worse cognitive performance in Atahualpa residents (Del Brutto, Gardener et al., 2014; Del Brutto, Peñaherrera et al., 2014).

2.5. Statistical analysis

Data analyses are carried out by using STATA version 15 (College Station, TX, USA). In univariate analyses, continuous variables were compared by linear models and categorical variables by χ^2 or Fisher exact test as appropriate. Using a generalized linear model, we evaluated whether the presence of ELC was associated with the MoCA score (dependent variable), after adjusting for demographics, cardiovascular risk factors, and edentulism.

In previous work conducted in Atahualpa, we noticed a strong interaction of age in several of the investigated variables (Del Brutto et al., 2017). Therefore, we anticipated a potential effect modification of age in the association between ELC and the MoCA score, and fitted models to assess the influence of age in this relationship. These included stratification of participants according to quartiles of age, and a exposure-effect model using augmented inverse probability weighting, which fitted a weighted regression model to obtain the average exposure effect of ELC over the MoCA score, after adjusting for covariates that were important for either the ELC and for the MoCA score.

3. Results

A total of 863 community-dwellers aged ≥ 40 years were enrolled in the Atahualpa Project from June 2012 to June 2017. At the time of the present study (August–September 2017), 170 individuals were no longer in the study because they had died, emigrated or declined consent. Of the 693 active individuals, 629 (91%) were included. Reasons for not participating included earlobe deformities precluding proper characterization of ELC in 42 individuals, and inability to perform the MoCA due to aphasia or severe visual or hearing impairment in the remaining 22 (Fig. 2).

Mean age of the 629 participants was 59.6 ± 12.3 years and 356 (57%) were women. A body mass index ≥ 30 kg/m² was noticed in 186 (30%) persons, blood pressure $\geq 140/90$ mmHg in 202 (32%), fasting glucose ≥ 126 mg/dL in 158 (25%), total cholesterol levels ≥ 240 mg/dL in 71 (11%), and severe edentulism (less than 10 remaining teeth) in 173 (28%). Twenty-three (4%) participants were current smokers, 28 (4%) had a poor diet, and 31 (5%) had poor physical activity. ELC was

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