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Inverse association between yerba mate consumption and idiopathic Parkinson's disease. A case–control study☆

Emilia Mabel Gatto [a,*], Carlos Melcon [b], Virginia L. Parisi [c], Leonardo Bartoloni [d], Claudio D. Gonzalez [e]

[a] Instituto de Neurociencias Buenos Aires, INEBA, Buenos Aires, Argentina
[b] Fundación para la Investigación en Neuroepidemiología (FINEP), Junín, Provincia de Buenos Aires, Argentina
[c] Departamento Neurología, Sanatorio de la Trinidad Mitre, Buenos Aires, Argentina
[d] Hospital A. Zubizarreta, Laboratorio de Investigación de la Memoria, Buenos Aires, Argentina
[e] Departamento de Farmacología, Facultad de Medicina, UBA, Argentina

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ABSTRACT

Yerba mate tea is a very common beverage in some countries of South America.
We conducted a case–control study on an individual basis using hospital records to investigate the association between Parkinson's disease (PD) and yerba mate intake. A case was defined as an age of ≥40 years with ≥1 year of PD. Each case was individually matched by two controls. Exposure was measured by yerba mate consumption, coffee, tea, and alcohol intake and smoking status.
The sample consisted of 223 PD patients (mean age 68 years and mean disease duration 7.3 years) and 406 controls. There was an inverse association between yerba mate "*bombilla*" consumption and PD (OR 0.64, 95% CI: 0.54–0.76, p = 0.00001). A multivariate analysis with a logistic regression adjusted by sex, alcohol intake and smoking provided the following results: yerba mate (OR 0.63, 95% CI: 0.53–0.76), tea (OR 0.60, 95% CI: 0.42–0.86), coffee (OR 0.51, 95% CI: 0.35–0.73).
We found an inverse association between yerba mate consumption and PD. These results led us to hypothesize that yerba mate may have a potential protective role in the development of PD.

1. Introduction

Although the etiology of Parkinson's disease (PD) is unclear, a combination of genetic, environmental and lifestyle factors have been proposed [1–7]. Some of these lifestyle factors might confer protection against PD [4]. Among the associated dietary factors, caffeine exposure appears to decrease the risk of PD [4]. An inverse association between coffee consumption and PD has been found in several epidemiological studies, with an observed dose and less probable gender effect [4]. A similar decreased risk of PD (RR) has been reported for cigarette smoking [8]. The apparent protective role of caffeine is mediated by an inhibition of adenosine A2A receptors, while a nicotinic effect has been proposed for tobacco exposure [9].

Interestingly, there are high levels of coffee use in most of the Americas and, in particular, in Europe (with a few notable exceptions). According to recent reports, people in Argentina drink little tea and only moderate amounts of coffee, but nonetheless, this country is one of the top consumers of hot, caffeinated beverages worldwide. Along with several of its neighbors, Argentina favors yerba mate (YM) [10].

YM tea or mate is an infusion made from dried, toasted and milled leaves and stemlets of the tree *Ilex paraguariensis* and is widely consumed in Argentina and other South American countries such as Brazil, Paraguay, and Uruguay (>27,900,000 individuals in Argentina have been estimated to consume YM) [11–13]. Mate drinking appears to have been widespread among the indigenous Guaraní and Tupi people in pre-Columbian times; Jesuit missionaries from Paraguay are generally credited with domesticating the plant [10].

Although yerba mate was limited to southern South America for a long time, in recent years, it has spread to other markets (United States, Middle East including Lebanon and Syria).

The health effects of yerba mate remain a topic of discussion, but studies have shown that mate can stimulate the central nervous system due to its content of methylxanthine alkaloids such as caffeine [14]. It is also known to contain compounds that possess antioxidant properties [14,15]. Mate has also been reported to have hepatoprotective, choleretic, diuretic, hypocholesterolemic, antirheumatic, antithrombotic, anti-inflammatory, antiobesity, and cardioprotective effects [16–19].

The bioactive compounds in YM (*Ilex paraguariensis*) include xanthines, phenolics, chlorogenic acid, theobromine, caffeine, chlorophyll, condensed tannins and saponins [15,20,21]. Experimental studies

☆ Contributors: Hernan Pavon, Jose Bueri, Nelida Garreto, Tomoko Arakaki, Marcelo Mattiazi.

* Corresponding author at: Juramento 1155 3°A, 1428 Buenos Aires, Argentina.
E-mail address: emiliamgatto@gmail.com (E.M. Gatto).

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suggest that hydroalcohol extract of yerba mate may have an antiparkinsonian profile [22].

The present case–control study was conducted in Argentina, and the main purpose of this study was to investigate whether there was an association between yerba mate consumption and the risk of Parkinson's disease.

2. Patients and methods

2.1. Study population

2.1.1. Subjects and methods

An observational analytical (case–control study) at a single base was performed to highlight and quantify the magnitude of the association between YM consumption and Parkinson's disease.

2.1.2. Source of information: Population database

PD cases and controls were recruited between April 1, 2011 and June 31, 2013 from 3 university hospitals, 1 national military hospital and 2 private institutions in the region of Buenos Aires.

The ethics committees of the 6 collaborating hospitals approved the protocol used for this case–control study.

2.1.3. Case

2.1.3.1. Case definition. Cases were defined as individuals aged ≥40 years at the time of inclusion with a diagnosis of idiopathic PD according to the diagnostic criteria of the London Brain Bank [23], with at least 1 year of disease progression and the capacity to answer a questionnaire. Onset was defined as the year during which one of the cardinal signs of the syndrome was first noticed by the patient or a care provider. The evaluation was conducted by a movement disorder specialist. Any other causes of Parkinsonism were excluded.

2.1.3.2. Case selection. Cases were selected by random sampling of the base population. We used as an alternative for the selection of prevalent cases, i.e., all (existing and new) assisted outpatient cases at the participating centers.

2.1.3.3. Case source. The cases stemmed from a "hospital source" cases and included centers of assistance that participated in the project (secondary study base).

2.1.4. Controls

2.1.4.1. Control definition. Control subjects were outpatients from the internal medicine department of each participant institution without a neurodegenerative disease. A preliminary selection was performed by medical records. Those with a history of Parkinsonian syndromes, first-degree family history of Parkinson's disease or other neurodegenerative diseases were excluded.

2.1.4.2. Control selections. Controls were selected by random sampling of the base population. The control group was a representative sample of the base population from which the cases were selected.

2.1.4.3. Control source. The recruitment of control subjects was conducted at the same collaborating hospitals.

2.2. Tools

2.2.1. Measurement of risk factors

After signed informed consent was obtained, a structured, in-person questionnaire, performed ad hoc, was administered by each one of the neurologist participants. The questionnaire elicited data on demographic variables, medical history, lifestyle factors, residential history, family history, educational level and environmental exposures (Table 1).

Table 1
Baseline characteristics of the study population.

	Case	Control	p value
Gender (F/M)	92/131	236/170	0.0001
Age (mean y)	68.03	66.20	0.039
Ethnicity (n)			0.259
Caucasian	207	389	
American-Indian	7	7	
Other	1	4	
Not available	8	6	
Never consumption (%)			
Tobacco	50	44.74	0.225
Tea	25.23	20.05	0.185
Coffee	11.71	6.36	0.033
Y mate	23.42	15.40	0.021
Alcohol	27.03	27.38	0.981
Educational level (%; expressed in years)			0.519
Null	0	0	
≤7 years	17.69	20.91	
7–12 years	38.82	32.73	
≥12 years	43	46.36	
No response	0.49		

2.2.2. Exposure estimation and definition of risk variables

The Spanish word *mate* refers not only to the dried leaves but also to the cup from which the beverage is drunk, which is traditionally a small hollow gourd. *Mate* is consumed in various ways as a tea, but the most popular method is by placing the *yerba mate* into the cup, pouring boiling water into it, and sipping the infused liquid through a straw called a *bombilla* (little pump). The *bombilla* acts as a filter—the end that goes into the liquid has a bulb pierced with small holes that prevents the leaves from traveling up the straw [13].

Subjects were queried about lifetime YM (mate bombilla or mate tea), tea and coffee consumption, the quantity (cups or ml/per day as appropriate, see Table 2), duration (in years) and frequency of consumption (days per month). Similar information for former users of YM, tea and coffee was considered taking into account years of consumption and years of intake discontinuation. Information on tobacco use included the number of cigarettes per day, years smoking started, and number of years smoked. Smokers were considered those who regularly or sporadically consumed snuff. Ex-smokers consisted of former smokers who quit smoking within one year prior to the survey and have not resumed smoking. No smoking consisted of individuals who ever smoked.

Information on alcohol consumption was determined from questions about typical consumption patterns such as the type of drink, quantity, and the time and frequency of consumption.

2.2.3. Reliability of information exposure

To complete the data collection questionnaire, all of the participants were surveyed in person by the study investigators.

2.2.4. Ascertainment of exposure

All of the participants completed a unique written questionnaire for the collection of individual data. Closed questions were used with

Table 2
Association between xanthine consumption and Parkinson's disease. Univariate analysis (univariate logistic regression).

Covariate	OR	95% CI	p value
Gender	1.94	1.31–2.88	0.0009
Tea cups/day	0.60	0.42–0.85	0.004
Coffee cups/day	0.50	0.35–0.72	0.0002
Mate bombilla (liters/day)	0.63	0.53–0.76	0.00001

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