

## The research on marijuana in Brazil

### *Pesquisas com a maconha no Brasil*

Surveying the research on marijuana in Brazil is a difficult undertaking, especially because until the 1950s or 1960s Brazilian scientific journals had an ephemeral life, were not indexed, and many of them cannot be found in libraries today.

In an incomplete review, the Brazilian Center of Information on Psychotropic Drugs (CEBRID, in the Portuguese acronym) listed a total of 470 Brazilian scientific articles related to marijuana published on the 20<sup>th</sup> and 21<sup>st</sup> centuries, only 39 of which were published until 1955. The two first articles date back to 1934 and were written by J. Lucena and published in the scientific journals *Arquivos da Assistência aos Psicopatas de Pernambuco* (Archives of Assistance to Psychopaths of the State of Pernambuco) and *Revista Médica de Pernambuco* (Pernambuco Medical Journal). Lucena and his colleagues were probably the most prolific researchers at that time, giving their State the deserved honor and describing the symptoms presented by marijuana users in the articles “Marijuanism and hallucinations”, “Marijuana smokers in Pernambuco”, “Chronic marijuanism and psychosis”, “Some evidence on marijuana smokers”, and others published in the previously mentioned journals and in *Revista Neurobiologia* (Journal of Neurobiology). It was at that time, between 1930 and 1940, that the repression to the use of marijuana gained strength in Brazil with the publication, by several Brazilian researchers, of articles with startling titles: “The evils of marijuana”, “Marijuana – Brazilian opium”, “The social dangers of marijuana”, “Toxicomanias”, “Marijuana intoxicated individuals in Porto Alegre”, “Addiction to Liamba in the state of Pará – a toxicosis that reappears amongst us”, etc.). In the same period, law enforcement actions were set off against marijuana breeders and users, supported by Federal Law Decree 891 of November 25, 1938.<sup>1</sup>

In 1956, the Ministry of Health, by means of the National Service for Sanitary Education and the National Committee for Narcotics Surveillance, organized what was probably the first national meeting on marijuana, and published a welcome issue with 28 articles on the topic.<sup>2</sup> All of the works describe and comment upon the effects of marijuana on users, without greater methodological detailing or experimental research results.

The authors from different Brazilian states reveal, as derived from the titles of their publications, a widespread attitude of that period: straight and simple criticism towards marijuana as if it

were a devilish drug (“Marijuana smokers: effects and evils of addiction”, “On the addiction to marijuana”, “Diamba addiction”, “Hemp or diamba and its intoxicating power”, “The social dangers of marijuana”, “Aspects of marijuanism in Sergipe”, “Diambism or marijuanism: murderous addiction”, “The toxic action of the marijuana produced in Brazil”, “Study on the nervous disorders produced by marijuana”, and others).

In the 1960s, the situation began to change with the pioneering studies of José Ribeiro do Valle, from the Escola Paulista de Medicina of the Universidade Federal de São Paulo (UNIFESP). This author sought, by means of animal experimentation, to quantify the effects of marijuana extracts and counted with the collaboration of S. Agurell, from Sweden, and B. Holmstadt, from Switzerland.

Valle also embraced many young Brazilians who began to show interest for the study of the plant. Thus was born the main and long-lasting group of research on marijuana, which continues today thanks to Valle’s “*children, grandchildren, and great-grandchildren*”. I had the honor of being one of the “children” bore at the Department of Pharmacology and Biochemistry of the Escola Paulista de Medicina. Encouraged by my “scientific father”, I was an intern for four years in the United States in order to learn “techniques on experimental psychology”, following his recommendation. The Section of Psychopharmacology was then founded, followed by the Department of Psychobiology, in 1973, which I came to head, concentrating the activities on animal research and on some experimental clinical trials with non-users of marijuana. In the 30 years that followed, 57 articles from this center were published, 42 of which in international journals such as *Psychopharmacology*, *European Journal of Pharmacology*, *Journal of Pharmacy and Pharmacology*, *Pharmacology*, *Biochemistry and Behavior*, *British Journal of Pharmacology*, and others.

Working in collaboration with chemistry groups from Israel (R. Mechoulam) and Germany (F. Korte) we demonstrated, in animals, that marijuana extracts -  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC), cannabidiol, and several other phytocannabinoids - were able to induce tolerance unrelated to LSD-25 and mescaline; that environmental stress enhanced some of the effects of marijuana; and that such compounds had marked hypnotic and anticonvulsant effects. It was also demonstrated that the levels of  $\Delta^9$ -THC could not be accounted for all the effects of the plant,

given the modulating action of cannabidiol over  $\Delta^9$ -THC. These studies have brought international recognition to the Department of Psychobiology, to the point of attracting interns or researchers in their sabbatical year from countries such as Uruguay (J. Monti), Argentina (I. Izquierdo), Greece (H. Savaki), and the United States (R. Musty, P. Consroe).

At the same time, several young Brazilians did internships or graduate courses at the Department of Psychobiology. Among “Valle’s grandchildren” were A. W. Zuardi, R. Takahashi, and I. Karniol, who returned to their places of origin and established productive research groups, especially at the Department of Behavioral Neurosciences of the Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo.

In 1984, the last two review articles of the Department of Psychobiology of UNIFESP<sup>3,4</sup> were published, one of which<sup>4</sup> remained on the list of the ten most accessed articles (“hottest papers”) of the journal *Toxicon*.

“Valle’s grandchildren”, especially A. W. Zuardi, continued their research on cannabinoids until the present time, with an emphasis on cannabidiol. In a recent review article,<sup>5</sup> many works published

by the Ribeirão Preto group were cited showing that this active principle of *Cannabis sativa L* has anxiolytic and antipsychotic properties, in addition to effects on motor disorders.

In fact, the Ribeirão Preto group, headed by Zuardi and including some of his former interns (“Valle’s great-grandchildren”) at their universities of origin, is today the most important group of research on cannabinoids in Brazil. As mentioned above, the authors of this group published almost 20 articles<sup>5</sup> focused on the action of cannabidiol and its possible therapeutic effects in the management of schizophrenia, anxiety, epilepsy, and motor disorders such as Parkinson’s disease. With the recent discoveries related to the existence of a complete cannabinoid system in the brain of mammals, including humans, it can be anticipated that “Valle’s great-grandchildren” will continue to make important contributions for the research in this field.

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#### Disclosures

Writing group member	Employment	Research grant <sup>1</sup>	Other research grant or medical continuous education <sup>2</sup>	Speaker’s honoraria	Ownership interest	Consultant/ Advisory board	Other <sup>3</sup>
Elisaldo A. Carlini	CEBRID	-	-	-	-	-	-

\* Modest

\*\* Significant

\*\*\* Significant: Amounts given to the author’s institution or to a colleague for research in which the author has participation, not directly to the author.

Note: CEBRID = Brazilian Center of Information on Psychotropic Drugs.

For more information, see Instructions for authors.

#### References

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