Registered Report

# Study protocol to assess sexual function in women of childbearing age with epilepsy

# Protocolo de estudo para avaliar função sexual nas mulheres em idade fértil com epilepsia

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**ABSTRACT | INTRODUCTION:** The diagnosis of epilepsy in women can trigger social, emotional, and sexual behavior changes. Studies have already shown that women in reproductive years with epilepsy are compromised in daily activities and quality of life due to their specificities. **OBJECTIVE:** To evaluate sexual function in women in reproductive years with epilepsy. **METHODS:** This is a sectional, descriptive and analytical study with a quantitative approach. Two groups of women will be analyzed: exposed group: with epilepsy and non-exposed group: without epilepsy. Data collection will take place by applying socioeconomic, demographic, and clinical questionnaires, Beck anxiety and depression inventory, Whooqol-*bref* to assess the quality of life, FSFI for sexual function, and FGSIS for the self-image of the genitalia. For data analysis, we will use association tests or verification of differences between parametric and non-parametric groups. In addition, the dependent variable sexual function will be tested for comparison with the independent variables. P <a 0.05 will be considered as a measure of significance. **EXPECTED RESULTS:** It is expected that factors associated with sexual dysfunction in women of childbearing age with epilepsy can be identified.

**KEYWORDS:** Epilepsy. Women. Sexual dysfunction.

**RESUMO | INTRODUÇÃO:** O diagnóstico de epilepsia em mulheres pode desencadear mudanças de comportamento social, emocional e sexual. Estudos já comprovaram que mulheres em idade fértil com epilepsia apresentam comprometimento no desenvolvimento das atividades diárias e na qualidade de vida devido às suas especificidades. **OBJETIVO:** Avaliar a função sexual nas mulheres em idade fértil com epilepsia. **MÉTODOS:** Trata-se de um estudo tipo transversal, descritivo e analítico com abordagem quantitativa. Serão analisados dois grupos de mulheres: grupo exposto: com epilepsia e grupo não-exposto: sem epilepsia. A coleta de dados se dará através de aplicação de questionários de dados socioeconômico, demográfico e clínico, Beck ansiedade e depressão, Whooqol-*bref* para avaliar qualidade de vida, FSFI para função sexual e FGSIS para autoimagem da genitália. Para análise dos dados, utilizaremos testes de associação ou verificação de diferenças entre grupos paramétricos e não paramétricos. A variável dependente "função sexual" será testada para comparação com as variáveis independentes. Serão considerados p< a 0,05 como medida de significância. **RESULTADOS ESPERADOS:** Espera-se que fatores associados a disfunção sexual em mulheres em idade fértil com epilepsia possam ser identificados.

**PALAVRAS-CHAVE:** Epilepsia. Mulheres. Disfunção sexual.

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## Introduction

Epilepsy affects about 6.38 per 1000 people.[1] It is a neurological disease characterized by the persistent predisposition of the brain to generate epileptic seizures, which may affect the individual's emotional, behavioral, cognitive, motor, and sensory state.[2] The impact of epilepsy goes beyond signs and symptoms, with the possible limitation of activities of daily living and consequent interference in the Quality of life.[3]

Abnormalities in sex steroid hormone metabolism (with androgen reduction) can affect many aspects of sexual functions. In addition, epilepsy can also induce comorbid neuropsychiatric disorders (i.e., depression and anxiety), which contribute to sexual dysfunction (SD).[4] Together, an increased rate of SD is expected in people with epilepsy. However, the results of different studies are controversial about the association between epilepsy and SD.[5]

Sexual function in women is complex and may be influenced by environmental factors, chronic diseases, previous sexual experience, tiredness, insecurity.[6] Women of childbearing age with epilepsy are a group that deserves a special look. The attention provided to this group cannot be focused only on the disease; these women present specific challenges and many particularities of roles and priorities related to the context in which their lives are present today, such as work, care for the family, and home.[7]

Thus, the present study proposes analyzing the primary outcome through assessing sexual function through the total score of the FSFI instrument (Female Sexual Function Index) in women of childbearing age with epilepsy. They are justified by the conflicting literature regarding the association of epilepsy with sexual function in women of childbearing age.[5] As secondary outcomes, the perception of the self-image of the genitalia, Quality of life domains, Anxiety scores will be analyzed in both groups with and without epilepsy; Depression scores associated with sexual dysfunction.

The recognition of sexual dysfunction in women of childbearing age with epilepsy may alert to the need for specific interventions with the potential to influence the Quality of life of this group.

## Methods

### Study design and period

An observational, cross-sectional, descriptive, and analytical study that will collect data with a quantitative approach. With collection from June 2019 to February 2021.

### Local

Epilepsy and Gynecology Outpatient Clinics.

### Target population

Women of childbearing age with and without epilepsy.

### Sample Selection

The available sample comprises an exposed group that will correspond to women registered and followed up at the epilepsy clinic and an unexposed group that will correspond to healthy women followed up by gynecology.

### Inclusion criteria

Exposed group:

a) women aged 18 to 44 years (fertile age, according to WHO)[8];

b) have a diagnosis of epilepsy according to the ILAE (International League Against Epilepsy)[9];

c) be able to answer questions;

d) agree to participate in the study by signing the Informed Consent Form (FICF).

Unexposed group:

a) women aged 18 to 44 years;

b) not having epilepsy;

c) be able to answer questions;

d) agree to participate in the study by signing the consent form.

**Exclusion Criteria**

Pregnant women, lactating women, active cancer undergoing treatment, stroke with motor sequelae and/or aphasia, high-grade brain tumor, and cognitive impairment that prevents answering the questionnaires, and those who do not complete the assessment steps will be excluded from the study.

**Statistical Assumptions**

Null Hypothesis (HO): There is no difference between the sexual function of women of childbearing age with and without epilepsy.

Alternative Hypothesis (HA): Epilepsy influences the sexual function of women of childbearing age.

Assessment instruments and variables to be studied

All participants will be guaranteed the Informed Consent Term, secrecy, confidentiality, and preservation in the analysis and processing of data. After signing the TCLE, in a single interview, the instruments will be applied on the dates scheduled for the service at the outpatient clinics in a reserved space, ensuring privacy and comfort, for an estimated time of 40 minutes, with no need for extra visits or visits outside the routine of care to complete filling out the questionnaires. If there is a need for a longer time to complete the instruments, the continuity of the research will be rescheduled for the date of the next return appointment, avoiding the need to return only for the research.

A brief recognition of each instrument and its variables follows:

1) Socioeconomic, demographic and clinical data questionnaire:

a. This questionnaire will collect the following variables: age, sex, marital status, education, profession/current occupation, personal income, family income, housing situation, comfort items.

b. If they have had sexual intercourse, they will answer the questions: last time their had sexual intercourse, monthly frequency of sexual intercourse in the last month, sexual orientation (homosexual, heterosexual or bisexual), number of partners, length of the relationship.

c. All respondents will answer about the presence of epilepsy (yes or no) or other comorbidities that will be self-reported as: clinical (high blood pressure, diabetes mellitus, hyperlipidemia, hypo/hyperthyroidism, obesity, smoking, have you ever had cancer? clinical?), psychiatric (do you undergo treatment? what type of treatment?) and/or neurological (headache/migraine, stroke? others?).

After collecting the information, the socio-economic classification will be carried out according to the Critério Brasil[10], stratified into classes A (highest), B1, B2, C1, C2, D, and E (lowest), revealing the income and power of purchase of research participants. It is noteworthy that this questionnaire composes the set of documents in the care of the epilepsy outpatient clinic and the Systematization of Nursing Care; however, in order to provide updates, this document will be revised and reapplied if necessary and will remain in the custody of the institution, ensuring the maintenance of follow-up and treatment by the health team.

2) Beck Anxiety and Depression Scales: these instruments are self-administered and will be evaluated exclusively by psychologists from the Epilepsy Outpatient Clinic.

3) WHOQOL-bref: This instrument broadly assesses QoL and can be applied to healthy people or people with health problems. Translated and validated for Brazil in 2000, the structure totals 26 questions related to the physical, psychological, social, and environmental domains.[11]

4) FSFI (Female Sexual Function Index): is an instrument translated and validated in Brazil since 2009 and assesses the Female Sexual Function Index. It contains 19 questions covering 6 domains: desire, excitement, lubrication, orgasm, satisfaction, and pain. Each question receives a score from 0 to 5, increasing concerning the presence of the questioned function. Only in questions about pain is the score defined oppositely. The questionnaire corresponds to the experience of the last four weeks. If the woman has not had sexual intercourse in this period, some answers will have this indication because the answer will be zero. The score of each domain is calculated by the sum of the belonging items multiplied by the corresponding factor. Domain scores are corrected and added, thus obtaining a total score that can vary between 2 and 36, being equal to or less than 26 indicates sexual dysfunction.[12]

5) FGSIS (Female Genital Self Image Scale): it is a reliable and widely used measure that enables the construction of a genital image in the current context. It is composed of 7 questions encompassing concerns about the appearance and function of a woman's genital self-image. In Brazil, it translates and validated in 2017.[13]

**Data Collection Procedures**

Private offices will be used, with the research participant and one researcher from the team in a confidential situation. The Beck Anxiety and Depression, FGSIS, and FSFI instruments are self-administered, but if necessary, the researcher will be available to clarify doubts or apply them in the form of an interview. Other questionnaires will be applied as individual interviews and filled out by the researcher (a) interviewer.

In case of emotional mobilization on the part of the research participant, a psychologist from the interdisciplinary team of the epilepsy clinic, as a matter of priority, or another duly qualified professional from the health team will provide immediate care. As already provided for in the service itself, a psychological follow-up routine can be maintained if a need is identified. Any participant who needs specific medical, psychological, or nursing follow-up will have this right guaranteed by the research team and the outpatient care team.

Complementary data related to epilepsy such as type, seizure control, medications used will be extracted from the electronic medical record after permission for the interview by signing the consent form. The storage of medical records will be subject to the conditions of confidentiality provided for all medical records of the institution. Their custody is established as recommended by RESOLUTION CFM 1821/07[14] - in its Article 7 - which refers to "permanent custody, considering the technological evolution, to patient records electronically filed in optical, microfilmed or digitized," and in its Article 8, which establishes the minimum period of 20 (twenty) years, from the last record, for the preservation of patient records on paper support, which were not electronically archived on optical, microfilmed, or digitized media.

The data collected during the interviews will be stored in the archives room that is kept locked in the Epilepsy Clinic, under the responsibility of the researchers for five years, and after this period, they will be permanently destroyed as recommended in Resolution 466 /12.[15]

**Data analysis plan**

It will be done by registering the questionnaires in a digital database using the Software Statistical Package for Social Sciences (SPSS). Data will be presented in distribution tables by the mean frequency and standard deviation for each group. For the quantitative study, data will be presented in tables by each group's mean frequency and standard deviation. The primary outcome (total score and FSFI domains) will be analyzed using the Mann-Whitney test to detect an association between groups with and without epilepsy. The Mann-Whitney test will also be used to detect the association of secondary outcomes: genitalia self-image and quality of life domains. We will use Fisher's Exact Test or Chi-Square to test the association between epilepsy and other secondary outcomes, such as socioeconomic, demographic, clinical (Anxiety and Depression scores), and sexual behavior of women of childbearing age. The association of clinical variables will also be tested: seizure control, type of epilepsy (focal and others), etiology (structural and others), presence of bilateral tonic-clonic seizures, use of medications (monotherapy or polytherapy), use of non-drug inducers, refractoriness and presence of side effects with the dependent variable: sexual function (total score and domains), through Mann-Whitney or Kruskal-Wallis. If any association between these variables appears, it will be adjusted using a logistic regression model to analyze the influence on sexual function and its domains in order to reduce confounding. Spearman's Correlation will test the Correlation between the sexual function domains with the self-image of the genitalia, Anxiety, and Depression scores, and Quality of Life domains.

The dependent variable sexual function will be tested for comparison with the independent variables (psychosocial and clinical data, anxiety and depression, WHOQOL-bref, FSFI, and FGSIS). $P< 0.05$ will be considered as a measure of significance.

The estimated sample size will be 55 women for each group, already considering a 10% loss, 5% significance level, and 90% power, totaling 110 participants. The sample size calculation was performed using total variability (considering that 49% of the patients have

a characteristic of interest and 51% do not) to detect a magnitude of the difference of 10% in the primary outcome. The primary outcome is the total sexual function score and follows a normal distribution concerning two standard deviations. Therefore, the standard deviation that will be considered for the analysis is 2, with the power to detect a difference of at most 2% between the groups in relation to the outcome since there is no theoretical basis; for this reason, the calculation was performed for an infinite population.[16]

**Scratches**

The following discomforts may occur: delay in the estimated time to answer the questions of the instruments that make up the study, which is an exclusive loss for researchers; because of the need for more time to apply the questionnaires, the continuity of the research will be rescheduled for the date of the next return appointment, avoiding the need to return only for the purpose of the research. In addition, the patient may feel embarrassed for not knowing or not getting the right answer to some of the questions asked or for personal-intimate questions, arousing emotions or facts experienced in their previous life. Since the entire research procedure will be done individually and the data are confidential and will not be disclosed individually, but, if necessary and deemed important, it will be welcomed by a psychologist from the interdisciplinary team of the epilepsy clinic, primarily, or another duly qualified professional from the healthcare team will provide immediate care. As already provided for in the service itself, a psychological follow-up routine can be maintained if a need is identified.

**Benefits**

The study will bring direct benefits: specific guidelines for health promotion and disease prevention related to women. About indirect benefits, it will bring social return through research procedures or products that will be freely available and contribute to improving services provided to this clientele. Therefore, there is no established remuneration, and no additional expenses are planned to participate in this research.

The monitoring of participants is independent of the study and will still be monitored by the institution after the end of the research. The results obtained will be disclosed to the public regardless of whether the results are favorable or not.

**Ethical aspects**

The project is approved by the Research Ethics Committee (CAAE nº 10533819.3.0000.5544). Patients will be invited to participate in the study voluntarily. During this entire period, they have the right to clarify doubts, to accept to participate in the research or withdraw the permission, at any time, without any kind of prejudice or repression for their decision, and may refuse to answer any question or withdraw the consent at any time, without prejudice to the relationship with the researcher or the institution. Moreover, Patients will be informed in detail about the research's objectives, procedures, risks, and benefits and will be guaranteed the confidentiality of their identities to preserve their image without causing harm.

## Expected results

Analysis of the resulting data will allow comparison between two groups of women of childbearing age. It will also permit us to assess the correlation between variables already tested in other studies, and, in addition, we will test variables not yet tested in the literature, such as the self-image of the genitalia and its relationship with quality of life.

It is known that women with epilepsy have worse quality of life when compared to women without it[17], but we do not know whether the sexual function can influence the quality of life. Few publications assess the sexual function in women of childbearing age with epilepsy in Brazil, thus providing new knowledge about this group.

### Author contributions

All authors were responsible for the conception and design of the study. Santos AMC wrote the manuscript. Castro-Lima H and Brito MB contributed to the critical intellectual content and final revision of the article.

### Competing interests

No financial, legal, or political conflicts involving third parties (government, companies, and private foundations, etc.) have been declared for any aspect of the submitted work (including, but not limited to grants and funding, advisory board participation, study design, preparation manuscript, statistical analysis, etc.).

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