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trends.denise@gmail.com

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Behs Jarros, Rafaela; Abrahão Salum, Giovanni; Tschiedel Belem da Silva, Cristiano;
Toazza, Rudineia; Becker, Natália; Agranonik, Marilyn; Fumagalli de Salles, Jerusa; Gus
Manfro, Gisele

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Attention, memory, visuoconstructive, and executive task performance in adolescents with anxiety disorders: a case-control community study

Desempenho em tarefas de atenção, memória, habilidades visuoestrutivas e funções executivas em adolescentes com transtornos de ansiedade: um estudo comunitário caso-controle

Rafaela Behs Jarros,^{1,2,3,4} Giovanni Abrahão Salum,^{1,2,4} Cristiano Tschiedel Belem da Silva,^{1,4} Rudineia Toazza,^{1,5} Natália Becker,³ Marilyn Agranonik,⁶ Jerusa Fumagalli de Salles,³ Gisele Gus Manfro^{1,2,4}

Abstract

Objective: The aim of the present study was to assess children and adolescents with mild and severe anxiety disorders for their performance in attention, verbal episodic memory, working memory, visuoconstructive skills, executive functions, and cognitive global functioning and conduct comparative analyses with the performance of children free from anxiety disorders.

Methods: Our sample comprised 68 children and adolescents aged 10 to 17 years (41 with current diagnoses of anxiety disorders and 27 controls) selected from a larger cross-sectional community sample of adolescents. Children and adolescents with anxiety disorders were categorized into two groups on the basis of anxiety severity (mild or severe). All participants underwent a neuropsychological assessment battery to evaluate attention, verbal episodic memory, working memory, visuoconstructive skills, and executive and cognitive functions.

Results: No differences were found in any neuropsychological tests, with the single exception that the group with mild anxiety had better performance on the Digit Span backward test compared to subjects with severe anxiety and to controls ($p = 0.041$; $\eta^2 = 0.11$).

Conclusions: Not only might anxiety disorders spare main cognitive functions during adolescence, they may even enhance certain working memory processes.

Keywords: Neuropsychological assessment, anxiety disorders, cognitive functions, adolescents.

Resumo

Objetivo: Este estudo objetivou avaliar crianças e adolescentes com transtornos de ansiedade leve e moderada nas funções neuropsicológicas de atenção, memória episódica verbal, memória de trabalho, habilidades visuoestrutivas, funções executivas e cognição global, comparando o seu desempenho ao de crianças com desenvolvimento típico.

Métodos: Participaram do estudo 68 crianças e adolescentes com idade de 10 a 17 anos (41 com diagnósticos clínicos atuais de transtornos de ansiedade e 27 controles), selecionados de uma amostra transversal mais ampla de adolescentes da comunidade. Os adolescentes com diagnóstico foram divididos ainda em dois grupos com base na gravidade dos transtornos (leve ou moderado). Todos os participantes realizaram uma avaliação neuropsicológica individual das funções de atenção, memória episódica verbal, memória de trabalho, habilidades visuoestrutivas, funções executivas e cognição global.

Resultados: Nenhum dos testes neuropsicológicos demonstrou diferenças significativas, sendo a única exceção a tarefa de *span* de dígitos ordem inversa, na qual o grupo com ansiedade leve apresentou desempenho superior ao do grupo com ansiedade moderada e também ao dos controles ($p = 0.041$; $\eta^2 = 0.11$).

Conclusão: Os resultados sugerem que não só os transtornos de ansiedade podem preservar as principais funções cognitivas durante a adolescência, mas que podem até melhorar certos processos de memória de trabalho.

Descritores: Avaliação neuropsicológica, transtornos de ansiedade, funções cognitivas, adolescentes.

¹ Programa de Transtornos de Ansiedade na Infância e Adolescência (PROTAIA), Serviço de Psiquiatria, Hospital de Clínicas de Porto Alegre (HCPA), Faculdade de Medicina, Departamento de Psiquiatria, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. ² Instituto Nacional de Psiquiatria do Desenvolvimento para Crianças e Adolescentes (INPD), São Paulo, SP, Brazil. ³ Núcleo de Estudos em Neuropsicologia Cognitiva (NEUROCOG), Departamento de Psicologia do Desenvolvimento e da Personalidade, Programa de Pós-Graduação em Psicologia, Instituto de Psicologia, UFRGS, Porto Alegre, RS, Brazil. ⁴ Programa de Pós-Graduação em Ciências Médicas: Psiquiatria, Faculdade de Medicina, UFRGS, Porto Alegre, RS, Brazil. ⁵ Programa de Pós-Graduação em Neurociências, Faculdade de Medicina, UFRGS, Porto Alegre, RS, Brazil. ⁶ Núcleo de Estudos em Saúde da Criança e Adolescente (NESCA), HCPA, UFRGS, Porto Alegre, RS, Brazil.

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Introduction

Anxiety disorders are very common psychiatric diagnoses among adolescents¹⁻³ and, unless adequately treated, they can seriously impair normal development⁴⁻⁷ and interfere with academic achievement and acquisition of social skills.

Many different mental processes have been associated with anxious behavior and some studies have suggested that neuropsychological assessment can be an important tool for increasing understanding of nosological aspects and treatment approaches in young people with anxiety.⁸ Whereas attentional bias related to emotional tasks is a core neuropsychological characteristic of anxiety disorders,⁸⁻¹¹ the role of other neuropsychological functions is less clear. In comparison with other psychiatric disorders in childhood, such as attention deficit hyperactivity disorder (ADHD), the relationships between anxiety disorders and impairments affecting broad high order cognitive functions are extensively under-investigated. Additionally, neurocognitive research investigating pediatric anxiety is underdeveloped compared to research into adult anxiety.¹² The majority of studies have investigated deficits in emotional processing rather than cognitive functions that can broadly impair emotional processing itself.¹³ Furthermore, evidence from comparisons of these neuropsychological characteristics in children and adolescents with and without anxiety disorders is mixed.

Some neuropsychological studies with children and adolescents have demonstrated that deficits in attention, memory, and academic performance may be associated with anxiety disorders.¹⁴⁻¹⁷ Deficits in spatial working memory performance have been related to childhood anxiety, but not to the same extent as is seen in ADHD.¹⁸ Specifically, social anxiety disorder (SAD) was associated with visual memory¹⁹ and executive functioning impairments according to severity,²⁰ and generalized anxiety disorder (GAD) was associated with deficits in attention.²¹ On the other hand, studies found no differences related to attention and verbal memory,²² or to performance monitoring and inhibition deficits,²³ in children and adolescents with anxiety disorders. These cognitive deficits can be explained in terms of an increased activation of threat-related representations and a failure to use controlled processing to support the activation of alternate non-threat-related representations, as described in the integrative theoretical framework.²⁴ Some findings indicate that inhibitory control is impaired in trait anxiety children but not in state anxiety subjects.²⁵ With regard to cognitive control processes (e.g., inhibition and working memory)

it is important to note that they develop at different rates and could be sensitive to emotional disruption.¹²

In view of the contradictory results, further studies to evaluate neuropsychological functions in adolescents with anxiety disorders might be helpful. Moreover, although findings related to attentional bias suggested that anxiety severity influences cognitive deficits,¹⁰ very few studies have evaluated the role of anxiety severity in other neuropsychological functions. The inconsistent results of these studies could be due to comorbidities and the clinical severity of patients with anxiety disorders. Moreover, data on the relationship between clinical severity and neurocognitive functioning is scarce.²⁰

Hence, the aim of this study is to compare the attention, verbal episodic memory, working memory, visuoconstructive skills, executive functions, and global cognitive functioning performance of individuals with mild and severe anxiety disorders to the performance of non-anxious controls in a community sample of adolescents. In view of what is reported by the studies reviewed, we expect to find that individuals with anxiety disorders have poorer performance, especially those whose symptoms are classified as severe.^{12,19,20,22}

Methods

Sample and procedure

Our sample was selected from a larger cross-sectional community sample comprising 10 to 17-year-old adolescents from six different public schools who were screened for anxiety using the Screen for Child Anxiety Related Emotional Disorders (SCARED).²³ A detailed description of the sample selection process can be found elsewhere.²⁶

Adolescents were diagnosed according to a clinical interview, followed by a semi-structured diagnostic interview based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), the Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (K-SADS-PL).²⁷ Six trained child psychiatrists or residents in psychiatry (kappa = 0.93 across anxiety disorders) were responsible for psychiatric diagnostic assessments. The K-SADS-PL was administered to the mother/father, followed by a direct interview with the adolescent. Best-estimate diagnoses were determined after a review of diagnoses, symptoms, and impairment levels by clinicians with experience in child psychiatry. Individuals were excluded if they had: 1) significant clinical illness; 2) history of affective bipolar disorder, pervasive developmental

disorder, or any psychotic disorder; 3) clinical suspicion of mental retardation and 4) were not treatment-naïve.

All non-medicated adolescents diagnosed with SAD, GAD, separation anxiety disorder, or panic disorder according to the diagnostic interview were selected as cases ($n = 41$). Moreover, individuals with anxiety disorders were categorized into two groups, based on the severity of their symptoms according to the Clinical Global Impressions (CGI): mild ($CGI \leq 4$) and severe anxiety ($CGI > 4$).^{28,29} Subjects with no anxiety disorders were considered controls ($n = 27$).

Adolescents diagnosed with specific phobia were considered cases only if the specific phobia occurred in comorbidity with any other anxiety disorder. Those with this condition alone were allocated to the control group, since specific phobia can be considered quite common during development, achieving spontaneous remission in most cases.³⁰ Individuals with: 1) history of clinical illness (i.e., hypothyroidism); 2) history of bipolar disorder, pervasive developmental disorder, or any psychotic disorder; and 3) clinical suspicion of mental retardation were excluded.

All subjects were contacted later to conduct the neuropsychological assessment at their schools. Their parents provided written informed consent for participation in the study; adolescents also provided written consent themselves. The Research and Ethics Committee at the Hospital de Clínicas de Porto Alegre (protocol no. 08593) approved this study.

Measures

Global cognitive functioning

We used the Wechsler Abbreviated Scale of Intelligence (WASI).³¹ This scale was developed to assess verbal, nonverbal, and general cognitive functioning and to exclude intellectual disability.^{32,33}

Attention

We used a cancellation task, the D2 test,³⁴ to evaluate visual focused attention. The subject is expected as quickly and accurately as possible to cross off the target (double-traced d letter) each time it appears. The score is obtained as the difference between the raw score and the total number of errors.

Working memory

We used the Digit Span forward (DSF) and Digit Span backward (DSB) subtests from the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV).³⁵ These subtests consist of eight digit sequences in the forward and seven in the backward directions, with a

gradual increase in the number of digits in each span. The maximum score in these subtests is 30, 16 for the forward and 14 for the backward sequences.³⁶

Verbal memory

Two instruments were used: the logical memory I and II subtests from the Wechsler Memory Scale, 3rd edition (WMS-III)³⁷ and the Rey Auditory Verbal Learning Test (RAVLT).³⁸⁻⁴⁰

The first of these tests was performed to evaluate the ability to learn and memorize conceptual material, presented in additive form. Subjects were asked to listen to a story and to recall it twice, first immediately and then again 30 minutes later. The maximum possible scores are 26 for the first story (A) and 25 for the second story (B).

The RAVLT consists of a single list of 15 words read loudly over five learning trials (I-V), which participants are required to freely recall after the administration of an interference list and after a 20-min delay. The RAVLT scores are the total number of words (maximum score: 15) recalled across five learning trials (I-V), the number of words (maximum score: 15) recalled following interference (VI) and the number of words recalled following a delay (VII).

Visuoconstructive skills and non-verbal memory

We used the Rey-Osterrieth Complex Figure test, which consists of copying and memory recall tasks using a complex geometric figure.⁴¹⁻⁴³ Subjects are asked to copy a complex figure (Rey-Copy) and then, without being told in advance, to reproduce it from memory (Delayed Recall).¹⁶ We assessed the precision and location of each part of the complex figure. The maximum score on each task was 35.

Executive functions

We used three instruments to assess executive functions. The first was a Go/no-go test, which is based on a paradigm of initiated or inhibited responses, depending on the stimulus that appears on a computer screen.^{44,45} Adolescents were asked to press a button whenever a blue N, J or W or a red, green or yellow O appeared on the screen and to inhibit a response whenever a blue O or a pink E were presented as stimuli. The score was based on their total hits (maximum score: 96).

The second instrument was the Wisconsin Card Sorting Task (WCST) - computer-based version - which involves evaluation of abstract reasoning, cognitive flexibility and shifting cognitive strategies in response to environmental contingencies.^{46,47} Participants are asked to match each card that appears in the center of the

screen to four different reference cards at the bottom of the screen. After matching each card to its corresponding reference card, participants receive positive (correct) or negative (incorrect) feedback. The pictures on the cards combine variations of shapes, colors, and numbers of figures printed. Subjects have to figure out the rationale behind combinations based on the computer feedback. Results are based on the total number of correct responses (maximum score: 60), perseverative errors (maximum score: 94), percent of conceptual level responses (maximum score: 100%), and number of categories completed (maximum score: 6).^{16,47,48}

The third executive function test was the Trail Making Test (TMT) A and B,⁴⁹ which is a test that evaluates processing speed, cognitive flexibility, visual search, and motor performance.⁵⁰ Adolescents had to draw lines to connect randomly disposed numbers, in ascending order, from one to 25. The second part of the test (Trail B) consisted of linking numbers (1 to 13) and letters (A-L) in alternate ascending order. Participants were given five minutes to complete each trail. Results reported for both TMT A and B are the number of errors and the time in seconds. In both cases, Trail A and Trail B, the maximum score is 24.

Statistical analysis

Data are expressed as means with standard deviations, and as relative and absolute frequencies. Analysis of variance (ANOVA) was conducted to compare neuropsychological performance results across the

three groups. Pearson's chi-square was used to identify associations for categorical variables. Variables with asymmetric distribution were square-root transformed.

All differences in neuropsychological performance between the three groups that had p values of less than 0.20 were included in a multivariate model of analysis of covariance (ANCOVA), controlling for possible confounders defined using the same statistical criterion or on the basis of theoretical relevance. Statistical analysis was performed using SPSS version 20.0 software. All tests were two-tailed and the effect size is presented as Partial Eta Squared. The overall level of significance adopted was $\alpha = 0.05$.

Results

Our sample comprised 68 participants, 41 adolescents with anxiety disorders (28 with mild and 13 with severe anxiety disorder) and 27 controls free from anxiety, who took part in the neuropsychological assessments. Anxiety diagnoses included GAD ($n = 29$; 69.0% mild), separation anxiety disorder ($n = 17$; 58.8% mild), SAD ($n = 16$; 43.7% mild) and panic disorder ($n = 2$; 100.0% mild). There were no significant differences between the three groups in age, gender, or sociodemographic variables. All groups were similar in terms of possible confounders, except for subjects with specific phobia, who differed significantly in terms of clinical severity (32.1% mild cases, 53.8% severe cases and 14.8% controls; $p = 0.037$) (Table 1).

Table 1 - Characteristics of anxiety and control groups

	Clinical Global Impressions - Anxiety			p-value
	Controls (n = 27)	Mild (n = 28)	Severe (n = 13)	
Age	12.6±1.96	13.0±2.19	12.2±1.21	0.397*
Sex				0.493 [†]
Female	9 (33.3)	8 (28.6)	2 (15.4)	
Grade				0.640 [‡]
4th	1 (3.7)	3 (10.7)	2 (15.4)	
5th	11 (40.7)	10 (35.7)	5 (38.5)	
6th	4 (14.8)	2 (7.1)	3 (23.1)	
7th	7 (25.9)	2 (7.1)	1 (7.7)	
8th	1 (3.7)	8 (28.6)	2 (15.4)	
1st to 3rd (high school)	3 (11.1)	3 (10.7)	0 (0)	
Socioeconomic status				0.837 [†]
High/intermediate	10 (37)	12 (42.9)	6 (46.2)	
Low	17 (63)	16 (57.1)	7 (53.8)	
Attention deficit hyperactivity disorder	9 (33.3)	4 (14.3)	5 (38.5)	0.153 [†]
Specific phobia	4 (14.8)	9 (32.1)	7 (53.8)	0.037 [†]
Oppositional defiant disorder	5 (18.5)	4 (14.3)	1 (7.7)	0.749 [†]
Depression	0 (0)	1 (3.6)	2 (15.4)	0.091 [§]
Post-traumatic stress disorder	0 (0)	0 (0)	1 (7.7)	0.191 [§]

Data presented as n (%) or mean ± standard deviation.

p-values: * analysis of variance (ANOVA); [†] Pearson's chi-square; [‡] Pearson's chi-square tendency; [§] Fisher's exact test.

In the bivariate analyses, participants with mild anxiety performed better in the Digit Span backward task than controls and than subjects with severe anxiety disorder ($p = 0.015$). There were no significant differences detected between mildly and severely anxious individuals and controls, even collapsing mild and severe groups into a single anxiety category.

Table 2 lists mean values for all neuropsychological tests for adolescents with mild and severe anxiety disorders and for those in the control group. We performed an ANCOVA in order to control for possible

confounders to our findings (age, gender, socio-demographic variables, WASI [total score], attention deficit hyperactivity disorder, and specific phobia). Even after statistical control the difference in the Digit Span backward persisted ($p = 0.041$; $\eta^2 = 0.11$), with a small effect size. The mild anxiety group had better performance than the other two groups, which, in turn, did not differ from each other. Although adolescents with severe anxiety had worse performance than the mild anxiety group, they did not have deficits when compared to controls.

Table 2 - Bivariate analysis comparing performance in neuropsychological tests across the three groups

Cognitive functions and tests	Clinical Global Impressions - Anxiety			F	p-value*
	Controls	Mild	Severe		
	(n = 27)	(n = 28)	(n = 13)		
	Mean \pm SD	Mean \pm SD	Mean \pm SD		
Attention					
D2	164.6 \pm 94.60	178.5 \pm 83.05	154.4 \pm 88.49	0.37	0.693
Working memory					
Digit Span forward	8.0 \pm 1.82	8.1 \pm 1.96	7.1 \pm 2.23	1.33	0.271 [†]
Digit Span backward	3.7a \pm 1.66	5.4b \pm 2.38	4.1a \pm 1.90	4.52	0.015 [†]
Verbal memory					
WMS A+ B (immediate)	21.2 \pm 5.35	23.4 \pm 7.19	21.2 \pm 8.71	0.85	0.434
WMS A +B (delayed)	18.3 \pm 5.41	21.5 \pm 6.45	18.5 \pm 7.23	2.03	0.140
RAVLT (1st list)	5.1 \pm 1.51	5.1 \pm 1.32	4.8 \pm 2.01	0.20	0.819
RAVLT (7th list)	10.0 \pm 2.65	10.0 \pm 2.91	9.1 \pm 2.05	0.69	0.507
Visuoconstructive skills					
Rey complex figure copy	27.5 \pm 5.00	30.0 \pm 4.44	30.6 \pm 3.81	2.94	0.060
Rey complex figure from memory	16.8 \pm 5.72	18.8 \pm 7.83	16.1 \pm 5.60	1.02	0.368
Executive functions					
Trail A (time)	66.5 \pm 20.95	61.1 \pm 18.35	72.4 \pm 22.46	1.45	0.243
Trail A (errors)	0.1 \pm 0.73	0.1 \pm 0.63	0.1 \pm 1.19	0.15	0.860 [†]
Trail B (time)	132.5 \pm 53.00	125.4 \pm 42.79	142.9 \pm 46.76	0.61	0.548
Trail B (errors)	0.2 \pm 1.25	0.1 \pm 1.21	0.3 \pm 1.29	0.42	0.662 [†]
Wisconsin - total number correct	81.1 \pm 11.85	78.6 \pm 13.17	77.7 \pm 13.53	0.43	0.655
Wisconsin - perseverative errors	17.3 \pm 6.76	18.3 \pm 9.52	20.7 \pm 9.68	0.72	0.489
Wisconsin - percent conceptual level responses	62.3 \pm 14.30	59.1 \pm 18.46	56.0 \pm 17.67	0.67	0.516
Wisconsin - number of categories completed	4.3 \pm 1.61	4.4 \pm 1.85	3.7 \pm 1.94	0.64	0.529 [†]
Go/no-go	82.1 \pm 5.61	80.3 \pm 7.25	80.5 \pm 8.03	0.54	0.583
Global cognitive functioning					
WASI	118.7 \pm 27.25	112.6 \pm 27.98	100.8 \pm 18.68	2.04	0.139

Data presented as n and mean \pm standard deviation.

F = F-statistic (F-ratio); RAVLT = Rey Auditory Verbal Learning Test; SD = standard deviation; WASI = Wechsler Abbreviated Scale of Intelligence; WMS = Wechsler Memory Scale.

* p-value according to analysis of variance (ANOVA); means followed by the same letter do not differ according to the test of minimum significant difference;

[†] p-value in ANOVA, square-root transformed.

Discussion

In contradiction of our initial hypothesis, we found no significant differences between the groups in most of the neuropsychological tests that were administered. Our study, in contrast with others,^{12,16,18,19} evaluated the participants using a large neuropsychological battery that covered many cognitive functions (attention, verbal

episodic memory, working memory, visuoconstructive skills, executive functions, and cognitive global functioning) within a small sub-sample from a larger, non-medicated, community sample diagnosed with anxiety disorders according to the DSM-IV criteria.

However, our study demonstrated that people with mild anxiety may perform better in the Digit Span backward, which is used to evaluate attention and

working memory, on the basis of comparison to controls and to a group with severe anxiety. Notwithstanding, subjects with severe anxiety did not outperform controls in the same task. This result did not corroborate our initial hypothesis and contrasts with findings from previous studies that have suggested that poor academic performance in children with anxiety could be partially mediated by a deficit in verbal working memory,⁵¹ since working memory has been found to be positively associated with learning ability and with academic achievement, especially in childhood.⁵¹⁻⁵³ Despite applying the same neuropsychological test, these authors did not evaluate clinical psychiatric diagnoses and neither did they rate anxiety severity.

Notwithstanding, studies have demonstrated that children with GAD may have poorer verbal memory, whereas children with social phobia may exhibit more omissions in a continuous performance task than healthy controls.¹⁶ Furthermore, we can hypothesize that adolescents with mild anxiety might have been more able to use their anxiety in a functional way as compared to adolescents with severe anxiety and controls, possibly mediated by better inhibitory control. In support of this last statement, previous studies have demonstrated an absence of inhibitory control impairment in state anxiety subjects.²⁵ Inhibitory control is one of the main functions of the prefrontal cortex and is important to the ability to resist task-irrelevant stimuli.⁵⁴ Additionally, we can also hypothesize that children with mild anxiety do not have amygdala hyper-responsivity and prefrontal under-recruitment.²⁴ Finally, in this study we did not attempt to evaluate the impact of socioeconomic status on the cognitive development of children with anxiety disorders.

Our research contributes important additional data to research into anxiety disorders, since all subjects were evaluated with extensive psychiatric assessments and neuropsychological testing. However, some limitations must be considered, such as the small sample size, which limits the statistical analyses. Furthermore, results were not controlled for multiple testing, which could have biased our positive findings. Additionally, it is important to note that our control group had other psychiatric comorbidities, which could have biased our results toward the null. Along the same lines, our sample had a significant burden of comorbidities, i.e., ADHD, which could influence the results. Specifically, with regard to ADHD symptoms it is important to point out that one third of our control group exhibited these symptoms. A recent meta-regression study concluded that global lifetime prevalence of ADHD was 9%,⁵⁵ lower than the prevalence observed here. Irrespective of this limitation, we statistically controlled our results for confounders, including ADHD, but it is important to hypothesize that

the mild anxiety group could have performed better in working memory tests because of its lower frequency of ADHD symptoms compared to the control group.

There is little evidence acquired by conducting neuropsychological testing in anxiety disorders among adolescents. The few studies that have been published report results for cognitive functions other than memory or attentional bias.^{8-11,16,19,22} Our study therefore provides preliminary evidence that neuropsychological deficits may not be remarkable features of anxiety disorders in adolescence. Future studies should increase sample sizes in order to be able to test with multivariate models, i.e., logistic regression, that could better explain the results reported here.

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Correspondence:

Natalia Becker
Universidade Federal do Rio Grande do Sul (UFRGS)
Rua Ramiro Barcelos, 2600, sala 114
90035-003 - Porto Alegre, RS - Brazil
Tel./Fax: +55 (51) 3308.5341 / +55 (51) 3023.6184
E-mail: natxib@gmail.com