

## Unpleasant Memories Related to Autobiographical Memory in Chronic Pain Patients

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### Abstract

**Purpose/ Aim of the study:** The objective of the present study is to analyze the aspects related to autobiographical memory in patients with chronic pain compared to a control group. In addition, an attempt was made to assess the variables that might influence autobiographical memory.

**Materials and Methods:** This was a case-control study conducted on patients with chronic pain and controls with no pain. Subjects included 29 patients with chronic pain and 29 control patients. Demographic data, clinical data related to pain, as intensity and use of analgesics, comorbidities, as depressive disorder and anxiety disorder, were assessed. Neuropsychological evaluation included the Montreal Cognitive Assessment and the Autobiographical Memory Test, Brazilian version.

**Results:** The main type of pain was lower back pain (31.0%), the mean current frequency of pain was  $22.3 \pm 10.8$  days/month, and mean pain intensity was  $8.1 \pm 1.6$ . Quantitative analysis did not differ significantly in the Montreal Cognitive assessment (22.5 versus 23.7;  $p = 0.18$ ), Autobiographical Memory Test words remembering (30.2 versus 31.8;  $p = 0.58$ ) and the latency time to respond (115.8 s versus 114.6 s;  $p = 0.42$ ). Qualitative analysis of memories evoked by neutral words revealed that chronic pain patients had more memories of negative content. These findings were not influenced by comorbidities.

**Conclusions:** The present results show that patients with chronic pain have changes in autobiographical memory compared to a control group, more specifically related to memory content (unpleasant memories) than to memory extension or latency time to assess memories.

**Keywords:** Chronic pain, Cognitive dysfunction, Comorbidities

## 1. INTRODUCTION

### 1.1. Chronic Pain

Painful syndromes continue to be a great challenge today, including various aspects such as intensity and associated manifestations, as well as subjective and multidimensional factors.<sup>1-3</sup> The prevalence of chronic pain defined for the general population by the World Health Organization (WHO) ranges around 37% in developed countries and 41% in developing countries.<sup>4</sup>

Chronic pain is a subject of research interest because it generates physical and emotional

stress for the patients and their caregivers, as well as financial and social losses for the population, including the treatment of pain and worker benefits due to physical disability.<sup>3-5</sup>

### 1.2. Autobiographical Memory and Chronic Pain

Patients with chronic pain frequently report cognitive complaints that cause difficulties in social situations and in daily life activities. Despite the considerable heterogeneity of the studies reviewed, there was a consistently significant result showing a better performance by healthy controls compared to patients with chronic pain in cognitive tests.<sup>6-9</sup> A 2013 meta-

analysis study systematically assessed the literature about working memory function in persons with chronic pain. This result can be explained by the network of activated brain areas in patients with chronic pain defined as pain matrix. Curiously, these brain areas include structures of the limbic system that are also involved in memory retention and fixation.<sup>8</sup>

More recently, two studies have assessed another cognitive strand in patients with chronic pain, i.e., autobiographical memory. This type of memory involves the memories of an individual about his own past at various levels of complexity, ranging from more generalized memories to specific life situations. These studies observed that the presence of pain resulted in loss of memory of autobiographical events in the life of an individual from both a qualitative and quantitative viewpoint.<sup>10-11</sup>

The hypothesis raised is that pain, as a complex and disagreeable emotional phenomenon, may prevent the access to more extensive memories related to previous experience and also to pleasant memories, and may also facilitate the memory of negative events, as unpleasant memories.<sup>10-11</sup>

Since mood disorders such as depressive and anxiety disorders may influence aspects related to memory and cognition<sup>12</sup>, these factors should be analyzed jointly in a study model aiming to assess the neuropsychological performance of patients with chronic pain. In addition, the medications used for the treatment of chronic pain and comorbidities may also affect the cognitive performance and should also be analyzed.<sup>13</sup>

Indeed, new aspects related to cognitive deficits of patients with chronic pain are being studied, indicating that new investigations should be devoted to such clinically relevant area. Thus, the objective of the present study was to describe and analyze the functioning of autobiographical memory in patients with chronic pain compared to control patients with no pain matched for sex, age and educational level. In parallel, the main factors that influence the cognitive disorders affecting the population with chronic pain were also assessed, as well as depressive and anxiety symptoms, use of medications and other comorbidities.

## 2. METHODS

This was a case-control study. Patients were recruited at a University Hospital for a period of six months. Patients aged 18 to 60 years with

non-oncologic chronic pain (lasting for more than 3 months)<sup>14</sup>, who agreed to give informed written consent were included in the study. They were recruited in the waiting rooms of the outpatient clinics of various specialties (orthopedics, neurology, internal medicine) by answering the question: "Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains and toothaches). Have you had pain, other than these everyday kinds of pain, in the last three months?". The exclusion criteria were the presence of mental changes that would prevent the response to a questionnaire and illiteracy.

### 2.1. Data Investigated

- 1) Demographic data such as age, sex, marital status, and profession.
- 2) A semi-structured questionnaire based on the Brief Pain Inventory<sup>17</sup> was applied to the patients with chronic pain. Clinical data regarding acute pain symptoms, location and characteristics of the pain, pain intensity (numeric pain scale), use of analgesic were obtained.
- 3) Comorbidities such as depressive disorder and anxiety disorder (Diagnostic and Statistical Manual of Mental Disorders 5 - DSM 5)<sup>18</sup>, sleep aspects ("Do you have any kind of sleep problems such as insomnia, unrefreshed sleep or sleep apnea?"), alcohol abuse ("How many doses of alcohol do you drink weekly?"), history of head trauma ("Have you ever had any kind of head trauma?") and other comorbidities that were previously diagnosed by other clinicians such as thyroid dysfunction, diabetes and hypertension.
- 4) Use of medication.
- 5) Neuropsychological evaluation by the Montreal Cognitive Assessment (MoCA) test and the Autobiographical Memory test, Brazilian version.<sup>15</sup>

Healthy patients matched for sex, age and educational level were recruited as controls. The study was approved by the Ethics Committee of the University Center Barão de Mauá (CAAE 54917816.7.0000.5378).

### 2.2. Brazilian Version of the Autobiographical Memory Test (AMT)

The AMT consists of the presentation of a series of stimulus-words of different emotional valences (positive, negative and neutral), with the participant being asked to retrieve specific memories of his life history related to these

words. The positive words used were Praise, Pleasant, Fun, Animated, and Honest, the negative words were Tragic, Unhappy, Misery, Angry, Disappointed, and the neutral words were Infantile, Moderate, New, Occasion, Rapid.

Taken together, latency time to a response and the results related to the specificity of the memories described represent the result of assessment.<sup>15</sup> (see table below). The Brazilian version of the AMT can be used in research on populations of low socioeconomic and educational level and has been used in Brazil in investigations related to dementia.<sup>16</sup>

In this study, interviews related to the application of the Autobiographical Memory test were recorded and later analyzed by two blind evaluators (a neurologist and a neuropsychologist), who did not know who were patients with pain and control patients, to establish quantitative scores and qualitative data analysis.

**2.3. Scores of the Brazilian Version of the Autobiographical Memory Test**

Category	Definition	Example	Score
Semantic associates	Response without reference to the past	Parties	0
Categorical memories	Memories of events with no defined beginning or end	When I go to a party	1
Extended memories	Memories of periods > 1 day	Parties during the first year of college	2
Specific memories	Memories of particular events	My graduation party	3

**3. STATISTICAL ANALYSIS**

Data were analyzed statistically using the SPSS software version 18.0.<sup>19</sup> Categorical variables were analyzed by the X<sup>2</sup> test or Fisher exact test according to the expected frequency in the cells. Quantitative variables were analyzed by the Kolmogorov-Smirnov test in order to define their type of distribution. Data with normal distribution were analyzed by analysis of variance (ANOVA) and data with non-normal distribution were analyzed by the nonparametric Mann-Whitney test. A linear regression model was used to correlate quantitative dependent variables controlled by independent variables, and a binary logistic regression model was used

to correlate dependent categorical variables controlled by independent variables.

**4. RESULTS**

Seventy patients were selected for the study. Two controls were excluded due to the presence of mental changes that prevented them from answering the questions and ten patients were excluded because they did not complete the interview. Finally, 29 patients with chronic pain (CPG) and 29 control patients (CG) were included in the study. The two groups did not differ in terms of age, educational level or gender (Table 1).

**Table 1.** Demographic data of patients with chronic pain (CPG) and control patients (CG)

	CPG / n= 29	CG / n= 29	p
Mean age	39.8 (Sd 11.0)	36.5 (Sd 11.1)	0,25**
Gender	21 (75.8%) women	19 (65.5%) women	0,56*
Up to 8 years of schooling	8 (27.5%)	8 (27.5%)	1,00*
> 8 schooling	21 (72.4%%)	21 (72.4%)	

\* Chi square \*\* Mann-Whitney test

The main types of pain, frequency and the mean intensity of pain according to the Numeric Pain Scale were described in Table 2.

**Table 2.** Chronic pain features

	Frequency
Pulsatile	9 (31.0%)
Pressure	6 (20.7%)
Burning	6 (20.7%)
Visceral	1 (3.4%)
Others	7 (24.1% )
Diagnostics	<b>Frequency</b>
Back pain	9 (31.0%)
Headache	5 (17.2%)
Osteomuscular pain	7 (24.1%)
Fibromyalgia	3 (10.3%)
Visceral pain	2 (6.8%)
Others	3 (10.3%)
Others	
Intensity- Numeric Pain Scale	8.1 (Sd 1.6)
Frequency (days/month)	22.3 (Sd10.87)

Regarding medication, 3 patients with pain (10.3%) used amitriptyline, 2 (6.8%) used other antidepressants, 1 (3.4%) used topiramate, 1 (3.4%) used gabapentin, and one (3.4%) used clonazepam. The analgesics more frequently used were dipyron (16, 44.4%) and non-hormonal anti-inflammatory (6, 22, 2%). The medications more frequently used by the controls were antidepressants (3, 10.3%) and clonazepam (1, 3.4%).

The comorbidities more frequently detected in CPG patients were generalized anxiety disorder (12, 41.4%), major depressive disorder (6, 20.7%), non-restoring sleep (10, 34.5%), hypertension (4, 13.8 %), diabetes mellitus (3, 10.3 %), and hypothyroidism (2, 6.8 %).

The comorbidities more frequently detected in CG patients were generalized anxiety disorder (10, 34.5%), non-restoring sleep (3, 10.3%), major depressive disorder (3, 10.3%), hypertension (1, 3.4 %), and hypothyroidism (1, 3.4%).

Patients with chronic pain did not show higher rates of anxiety disorder (p= 0.78) or depressive disorder (p= 0.47).

Quantitative assessment results of the neuropsychological tests applied revealed no differences in scores for chronic pain group, comparing to a control group, in the MoCa Test (22.5 versus 23.7; p = 0.18), remembering autobiographical memories - positive, negative and neutral emotional valences and in the latency time in responding questions - positive, negative and neutral emotional valences (see scores in Table 3).

**Table3.** Chronic pain patients (CPG) and control group (CG): Autobiographical Memory Test Brazilian version scores (positive, negative and neutral emotional valences: remembering autobiographical memories and latency time in responding questions)

Autobiographical Memory Test	CPG n = 29	CG n =29	P *
Positive valences	10.4	11.1	0.84
Positive valences – latency time**	26.1	22.6	0.88
Negative valences	10.9	11.1	0.84
Negative valences – latency time**	28.0	26.5	0.68
Neutral valences	8.9	9.5	0.89
Neutral valences – latency time**	45.8	39.5	0.98
Sum valences	30.2	31.8	0.58
Sum valences – latency time**	115.8	114.6	0.42

\* Mann-Whitney test \*\*seconds

Regarding the qualitative assessment of neuropsychological tests applied, when we evaluated the memories evoked by neutral words, we observed that CPG patients had a distorted view of remembered memories, with a larger number of memories with a negative content (unpleasant memories) than CG patients for the words “Infantile” and “Rapid” (Table 4). To assess the content of memories (negative or not) evoked by the words “Infantile” and “Rapid”

controlled for the independent variables chronic pain, depressive disorder and anxiety disorder, we used a binary logistic regression model (Tables 5). Chronic pain was an independent factor for the results obtained.

**Table4.** Number of negative (unpleasant) memories evoked by neutral words, in chronic pain group (CPG) and control group (CG)

Neutral words	Negative (unpleasant) Memories		P *
	CPG	CG	
Infantile	11	6	0.00
Moderate	8	7	0.32
New	5	5	0.97
Occasion	7	5	0.08
Rapid	15	8	0.02

**Table5.** Linear regression model, where words “Infantile” and “Rapid” were dependent variable, controlled for the independent variables Chronic Pain, Depressive Disorder, Anxiety Disorder.

Model 1 : Infantile	Unstandar -dized Co-efficients B	Odds ratio adjusted OR	95% confidence interval for B		P *
Chronic Pain	-2.13	0.12	0.04	0.40	0.00
Depressive Disorder	0.05	1.05	0.18	6.21	0.95
Anxiety Disorder	0.82	2.27	0.60	8.59	0.23
Model 2: Rapid					
Chronic Pain	-1.90	0.15	0.02	1.00	0.05
Depressive Disorder	-0.12	0.89	0.06	12.34	0.93
Anxiety Disorder	0.58	1.79	0.30	10.76	0.52

## 5. DISCUSSION

The present study described and analyzed cognitive aspects related to autobiographical memory in patients with chronic pain and in controls with no pain paired for sex, age and educational level, in addition to assessing the main factors triggering the cognitive disorders observed such as depressive disorder and anxiety disorder.

Cognition and chronic pain represent a topic currently under study and the possible reasons for cognitive deficits include the presence of depressive symptoms (which are detected in 40 to 58% of patients with chronic pain) and the use of medications.<sup>20</sup> However, other studies have reported that chronic pain may be an independent factor for cognitive deficits.<sup>9</sup>

Within this context, according to previous studies<sup>10-11</sup>, autobiographical memory may also be influenced by the presence of chronic pain. It has been reported that patients with chronic pain may have a lower memory index for autobiographical events, as well as a longer latency time to start remembering these events. Another aspect studied is the distortion of these remembered memories in patients with chronic pain, who tend to remember more events with a negative emotional valence.<sup>10-11</sup>

In the present study, we observed that a group of patients with chronic pain showed worse absolute scores than a control group in the autobiographical memory test, and a longer latency time to respond to all emotional valences (positive, negative and neutral). However, as also reported by others,<sup>11</sup> the results obtained were not statistically significant. The first possible justification of these findings could be that the small number of patients studied was insufficient to detect the expected results. In addition, similar results were obtained with the MOCA test, although in larger groups of patients differences between patients with chronic pain and controls with no pain have been previously reported by our group.<sup>9</sup>

A second possibility is that control patients may also perform poorly in these types of tests with an abstract content since their educational level is also low, especially in our country. Since there are very wide variations in performance in this type of test, which is extremely subjective, and the low educational level in developing countries may influence the results, our findings may differ from the studies published in developed countries on samples of better socioeconomic and cultural level.

Regarding qualitative memory assessment, we detected a larger number of memories of negative content (unpleasant memories) when evoked by neutral words in patients with chronic pain, regardless of the presence of anxiety or depressive disorder. This finding demonstrates a distortion of described memories in patients with chronic pain, as also reported in a previous study<sup>10</sup>. This distortion of memories may be related to pain catastrophizing which is one of the stronger psychological predictors of the description of pain by the patients.<sup>21</sup> In patients with chronic pain, "catastrophization" is defined as an exaggerated negative cognitive-affective orientation in relation to pain. Some studies have also detected a lower performance in neuropsychological tests associated with greater

pain intensity and catastrophization.<sup>22</sup>

Regarding the clinical implications of these findings, there is evidence of moderate and high quality using cognitive-behavioral therapy, multimodal treatment and mindfulness-based stress reduction for an improvement of catastrophizing symptoms, besides increasing patient self-efficacy for managing pain and pain acceptance.<sup>21;23</sup> On this basis, it would be interesting to define a battery of tests that might identify the patients with these symptoms and refer them to proper treatment.

Thus, although the present study was a small one, we consider the demonstration of these findings to be pertinent for several reasons. First of all, no previous study has been conducted in Brazil to analyze autobiographical memory in patients with chronic pain. Secondly, there is the possibility to treat the symptoms of these patients, with a possible reduction of suffering and an improvement of the quality of life of these patients.

We may also suggest to other investigators to repeat these studies on a larger number of patients for a better definition of the quantitative analysis of the memories reported. In any case, the model of neurocognitive changes associated with chronic pain is still far from being fully understood.

In conclusion, the results lead us to believe that patients with chronic pain have cognitive changes related to autobiographical memory. These changes are more related to evoked memory content (unpleasant memories) than to memory extension (quantitative description) or latency time to evocation.

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