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COGNITIVE-BEHAVIORAL INTERVENTION

TO MODIFY RUMINATIVE RESPONSES AND PLASMA IL-6 IN COLLEGE STUDENTS WITH DEPRESSIVE SYMPTOMATOLOGY

INTERVENCIÓN COGNITIVO-CONDUCTUAL PARA MODIFICAR LAS RESPUESTAS RUMIATIVAS Y LA IL-6 PLASMÁTICA EN ESTUDIANTES UNIVERSITARIOS CON SINTOMATOLOGÍA DEPRESIVA

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ABSTRACT

Evidence suggests that ruminative responses, or rumination, are a predictor, exacerbated, and residual symptom of psychopathologies, especially depression. A common approach is observed, researchers are not focused on previously created interventions to know how to reduce and replace rumination to prevent the development of psychopathologies. Cognitive-behavioral techniques have been demonstrated to be useful to decrease repetitive thoughts. Interleukin-6 (IL-6), a proinflammatory cytokine, is present in plasma from persons with depression so it can be used as a biomarker. The present study was conducted to decrease ruminative responses and plasma IL-6 in depressed college students. For this purpose, participants meeting the criteria for "rumination" according to "Ruminative Responses Scale" (n=3) were chosen. In general, the study of a single case with two repetitions demonstrated a decrease of ruminative responses, depressive symptomatology, and plasma IL-6. These data are consistent with previous studies.

Keywords: Ruminative responses, depressive symptomatology, plasma interleukin-6, cognitive-behavioral intervention, college students.

RESUMEN

La evidencia sugiere que las respuestas rumiativas, o la rumiación, son un síntoma predictor, exacerbado y residual de psicopatologías, especialmente de depresión. Se observa un enfoque común, los investigadores no se centran en intervenciones creadas previamente para saber cómo reducir y reemplazar la rumiación para prevenir el desarrollo de psicopatologías. Se ha demostrado que las técnicas cognitivo-conductuales son útiles para disminuir los pensamientos repetitivos. La interleucina-6 (IL-6), una citocina proinflamatoria, está presente en el plasma de personas con depresión, por lo que puede usarse como biomarcador. El presente estudio se realizó para disminuir las respuestas rumiativas y la IL-6 plasmática en estudiantes universitarios deprimidos. Para ello, se eligieron los participantes que cumplían con los criterios de "rumia" según la "Escala de Respuestas Rumiantes" (n=3). En general, el estudio de un solo caso con dos repeticiones demostró una disminución de las respuestas rumiantes, la sintomatología depresiva y la IL-6 plasmática. Estos datos son consistentes con estudios previos.

Palabras clave: Respuestas rumiativas, sintomatología depresiva, interleucina-6 plasmática, intervención cognitivo-conductual, estudiantes universitarios.

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INTRODUCTION

Depression is a significant public health problem, which affects from 1 to 10% of the worldwide population, but in college students, the rate is more elevated: 20 to 30% because they live in a particular stage: emerging adulthood. It is not about extended adolescence, since they are not minors, and they still do not have all the responsibilities of adults, which places them in a particular stage (Arnett, 2016; Cook, et al., 2019; Schwartz & Petrova, 2019; United Nations Policy Brief, 2020). Researchers have indicated that emerging adults face up to choose to go to college or get a job, get married, choose a career, know how to use the money, have long and significant relationships, etcetera. All these issues are stressful by themselves, but when they come together in young persons, they may favor the development of depression due to diverse style responses to sadness or stress. According to "Response Style Theory," a maladaptive response is rumination, and adaptive responses are solving problems and distraction (Arnett, 2016; Cook, et al., 2019; Rosenkranz, et al., 2020).

Many emerging adults respond to stressful events through ruminative responses or rumination, a series of repetitive and intrusive ideas about their sadness, causes, and possible consequences (Cook, et al., 2019). Rumination is a predictor and exacerbation of psychopathologies such as depression or anxiety. Also, it remains a residual symptom of depression; thus, persons with ruminative responses have more depressive episodes than those who have not (Watkins, 2008; Spinhoven, et al., 2017; Rosenkranz, et al., 2020).

Rumination is challenging to be changed because people think it is useful; then, overthinking the same issues may look positive because people are looking for a solution to sadness, but this is not true. These people are passively thinking, but they cannot do what they are thinking. Although there are programs to prevent depression, they may constantly be improved; in fact, efficacy improves if it targets interventions as specific risk factors, such as rumination. Cognitive-behavioral interventions have been demonstrated to be the most effective to reduce rumination because they substitute repetitive thoughts for techniques as a distraction or solving problems (Hollo et al., 2021).

Techniques were carefully chosen to reduce or substitute the ruminative responses. *Psychoeducation* supports a better understanding of what rumination and depression are, *solving problems* and *distraction* to increase adaptive responses according to the "Response Style Theory," *behavioral activation* to prevent avoidance behaviors, *cognitive restructuring*, and *mindfulness* to substitute the repetitive thoughts. These techniques have been applied individually in different groups (such as women with cancer, teenagers, college students, and persons with depression), and each one had demonstrated to be effective in all cases (Perestelo-Pérez, et al., 2017; Spinhoven, 2018; Cladder-Micus, 2019). Nevertheless, it was essential to prove their effectiveness as a group of techniques.

Besides, scientific evidence has shown that interleukin-6 (IL-6), a proinflammatory cytokine, is a biomarker of depression: plasma levels in healthy persons are undetected while in someone with depression are elevated (Hodes, et al., 2016; Ng, et al., 2018; Roohi, et al., 2021).

The intervention was built to reduce ruminative responses and substituted for cognitive-behavioral techniques. IL-6 was used (besides psychometric tests) as a biomarker to assess its effectiveness. The cognitive-behavioral techniques chosen (psychoeducation, distraction, solving problem, behavioral activation, mindfulness, and cognitive restructure) were able to reduce rumination, IL-6, and depressive symptomatology (Querstret & Cropley, 2013; Dimidjian, et al., 2014) (Table 1).

Table 1. Cognitive-behavioral techniques chosen to reduce rumination, IL-6 and depressive symptoms.

Sessions	Techniques	Objective
Session 1	Psychoeducation	Setting the rules. Knowing what rumination and depression are. Emotional control.
Session 2	Cognitive restructuring	Identify ruminative responses and irrational. Decrease them.
Session 3	Behavioral activation	Decrease rumination and depressive symptomatology.
Session 4	Distraction	Decrease rumination.
Session 5	Solving problems	Increase abilities to solve problems.
Session 6	Mindfulness	Emotion control. Substitute rumination for mindfulness.

MATERIALS AND METHOD

All subjects were applied for being in the "Psychology Attention Clinic." They filled out a psychology battery with the "Ruminative Responses Scale" (RRS) and "Beck Depression Inventory" (BDI). Participants were selected by a high score in both tests, which were administered among students from the Autonomous University of State of Hidalgo. Persons meeting the criteria for depressive symptomatology and ruminative responses were invited to participate.

Fifteen students were chosen, but only five had achieved the inclusion criteria. All the participants started the intervention, but two participants did not finish the treatment because of the vacation season. The final sample was constituted of three students (two men and one woman) of the psychology career with a mean of 19 years.

A single case design was selected because of the sample size, and this was the most relevant design to understand the effect of a particular treatment (Kazdin, 1982), where every subject is his or her control. This design combines clinical treatment and research; first, a baseline was elaborated, and then an intervention was applied to identify the changes.

The BDI for the Mexican population (Jurado, et al., 1998) is a 21-item-self-reported-questionnaire, which measures depressive symptomatology in the last week to completion of the questionnaire. Persons with scores higher than ten and under 30 were selected to participate. Psychometric characteristics of the BDI have been investigated in different languages and countries (Beck, et al., 1961).

The RRS was developed by Nolen-Hoeksema (1991). It is a 22-item-self-reported questionnaire that measures ruminative responses in the last week. The persons qualified with scores higher than 40 present them. It has three components: reflection, brooding, and depression. The RRS possesses adequate validity and reliability (Treynor, et al., 2003). The RRS for the Mexican population was validated in 2017 (Hernández-Martínez, et al., 2017).

Subjects were instructed about the procedure at arrival, and their informed consent was obtained. Subsequently, a qualified nurse collected a blood sample (5 mL) from every participant using a syringe containing sodium heparin anticoagulant. After that, the participants had a small break and went to their classroom. The blood samples were centrifuged at 3000 rpm for 10 minutes; each plasma was divided into three parts, frozen, and kept at -70 °C. Two samples were kept, and the other one was used to quantify the levels of IL-6 with the high sensitivity ELISA test (greater than 0.1 pg/mL) Clayton trademark. Plasma IL-6 from healthy persons resulted undetected, while depressive subjects got a mean of 6.98 pg/mL.

Then, they participated in an individual cognitive-behavioral intervention of one hour per week for six weeks. The techniques learned were psychoeducation, distraction, solving problems, cognitive restructuring, behavioral activation, and mindfulness. Finally, after six weeks, the nurse collected again blood samples that underwent the process mentioned above.

For the statistical analysis, the program SPSS 23 version was used. A test of Friedman was employed to find the difference between the psychological tests. Besides, to analyze the difference in plasma IL-6 concentrations, the t-Student test was used. Besides, for the behavioral changes in every subject, "Split-middle-technique" was employed (Kazdin,1982). For the results of the Friedman's test and t-Student, a significance of 0.003 was considered. In the case of "Split-middle-technique," the significance employed was 0.000.

RESULTS AND DISCUSSION

The differences between groups were observed by comparing them before and after the intervention. Variables showed a decrease in their values: depressive symptomatology (MD= 17.3 vs. MD=6.67). Ruminative responses (MD= 57.33 vs MD=39) and IL-6 (MD=6.981pg/mL vs 0 pg/mL) (Tables 2, 3 and 4).

In this statistical technique, each subject is his control. The variable to change is measured before and after the intervention to know if it increased or reduced. In this case, ruminative responses were the variable measured every day until the intervention finished (MD=4 vs. MD=0).

Plasma IL-6

The differences in the level of plasma IL-6 before and after the intervention were statistically significant: before the intervention, the mean was 6.981 pg/ml, and after was 0 pg/mL.

Table 2. Levels of ruminative responses before and after the intervention.

Participants	Ruminative responses Pretest	Ruminative responses Postest
Participant 1	64	46
Participant 2	51	24
Participant 3	57	47

Table 3. Levels of depressive symptomatology before and after the intervention.

Participants	Depressive Symptomatology Pretest	Depressive Symptomatology Postest
Participant 1	17	5

Participant 2	18	0
Participant 3	17	15

Table 4. Levels of plasma IL-6 before and after the intervention.

Participants	Levels of IL-6 (pg/mL) Pretest	Levels of IL-6 (pg/mL) postest
Participant 1	15.272	0
Participant 2	6.863	0
Participant 3	6.636	0

The present study found clear indications that participants significantly reduced their levels of depressive symptomatology, ruminative responses, and plasma IL-6 using techniques that were thought helpful in the cognitive-behavioral field. These results are according to the literature were the most effective techniques are the cognitive-behavioral including mindfulness (Frick, et al., 2020).

WHO has claimed that it is necessary to create and apply programs to prevent depression to avoid its fatal consequences, such as suicide. Nevertheless, although there are many programs, rumination in depression as the primary target is urgently required. Results have demonstrated its effectiveness in college students; indeed, they reduced repetitive thoughts and learned how to substitute them with techniques that improve their quality of life (Cook & Watkins, 2016; Tesoro, et al., 2021).

However, it is important to take into account the scope of this study and that it can also be identified as one of its limitations. This intervention was designed as a case study with two replicates, so the individual intervention limits the possibility of generalizing the results, and its effectiveness should also be tested if it were applied in a group manner. On the other hand, it is important to go beyond the pre-post evaluation and consider that the follow-up after finishing the intervention could help to identify the medium and long-term effect of the intervention.

Follow-up evaluations would also allow knowing the evaluation of ruminative thoughts and identifying if these can be kept at low levels that do not cause emotional discomfort to the participants or if they increase over time, favoring the presence of symptoms or a relapse in the following months or years. The characteristics of the participants should also be considered, since they were young university students, so it would be important to test the effect of the intervention in other age groups as well. Since the effectiveness of the intervention could vary in older or younger people and with different school levels, that is why it will be important to make adjustments to the proposal that are appropriate for the characteristics and needs of other populations.

CONCLUSIONS

After carrying out this intervention, it can be concluded that the participants presented a decrease in depressive symptoms, also observing changes in their IL-6 levels, which is linked to a lower inflammatory process.

These types of proposals are easy to apply, low cost and highly effective, so they can be considered as intervention strategies in highly vulnerable scenarios such as universities, schools, sports or spaces where young people carry out academic or exercise activities, which would facilitate quick and timely access to mental health care services. Unfortunately, one of the main limitations to carry out studies with biomarkers continues to be the poor accessibility or the limitations in terms of material resources that are experienced in research spaces and that increase when clinical psychologists want to use them in clinical settings without funding or where They must work with limited resources.

The benefits of cognitive behavioral therapy are clear, however, few studies emphasize the use of biomarkers as measurement elements associated with clinical change, so this is a relevant contribution that can serve to improve psychological evaluations in future studies or clinical interventions.

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