Relationship between emotion and health: a two-way street

Relação entre emoção e saúde: uma via de mão dupla

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Elsa Santos Lima
Master student in Bioinformatics
Institution: Universidade Federal do Paraná (UFPR)
Address: R. Roraima, 2096, Curitiba – PR, CEP: 82930-000
E-mail: elsalimma@gmail.com

Camila Pereira Perico
Master in Bioinformatics by Universidade Federal do Paraná (UFPR)
Institution: Laboratório de Inteligência Artificial Aplicada à Bioninformática - Universidade Federal do Paraná
Address: Rua Alcides Vieira Arcoverde 1225, Curitiba - PR, CEP: 81520-260
E-mail: camilapp94@gmail.com

Bruno Thiago de Lima Nichio
Doctor of Science
Instituição: Laboratório de IA Aplicada a Bioinformática - Universidade Federal do Paraná (UFPR)
Endereço: Rua DR Alcides Vieira Arcoverde, 1225, CEP: 81520-260
E-mail: brnichio@ufpr.br

Reginaldo Daniel da Silveira
PhD in Production Engineering: Media and Knowledge from Universidade Federal de Santa Catarina (UFSC)
Institution: Centro Universitário Internacional (UNINTER)
Address: Rua Prof. Pedro Viriato Parigot de Souza, 1100, Bloco 6, Mossunguê, Curitiba – PR, CEP: 81200-100
E-mail: reginaldodaniels@gmail.com

Roberto Tadeu Raittz
PhD in Production and Systems Engineering by Universidade Federal de Santa Catarina (UFSC)
Institution: Universidade Federal do Paraná (UFPR)
Address: R. Theodoro makiolka, 1060, Casa 24
E-mail: raittz@gmail.com

Dieval Guizelini
PhD in Sciences-Biochemistry
Institution: Universidade Federal do Paraná (UFPR)
Address: R Guararapes, 2270, Curitiba – PR, CEP: 80320-210
E-mail: dieval@ufpr.br

Luiz Antonio Pereira Neves
Postdoctoral Fellowship in Computer Vision and Robotics
Institution: Universidade Federal do Paraná (UFPR)
Address: R. Dr. Alcides Vieira Arcoverde, 1225, Jardim das Américas, Curitiba - PR, CEP: 81520-260
E-mail: lapneves@gmail.com

Jeroniza Nunes Marchaukoski
PhD in Medical Informatics
Institution: Universidade Federal do Paraná (UFPR)
Address: R. Dr. Alcides Vieira Arcoverde, 1225, Jardim das Américas, Curitiba - PR, CEP: 81520-260
E-mail: Jeroniza@gmail.com

ABSTRACT
Emotional reactions impact on people's health and quality of life. With the advent of neuroscience in the 1990s, much research has focused on the relationship between neural circuits and emotional reactions. In this sense, we have identified a 2031% growth in research linking emotions and health between 1990 and 2022. Using the Text mining tool called "Biotext Tools", we performed a literature search, focusing on diseases of old age and covid-19. Emotion molecules (EMs), produced by the endocrine system, impact the homeostasis of the body, affecting the biological balance of the body. We related the EMs with diseases of the elderly and Covid-19, in order to analyze the impact of emotional states on the development and treatment of these pathologies. To this end, the bidirectional relationship between anxiety, depression, heart disease, stroke, and Alzheimer's and Parkinson's diseases was analyzed. Finally, Coronavirus severity and mortality levels were related to cortisol, testosterone, and serotonin levels.

Keywords: emotion, health, diseases, molecules, endocrine, elderly, COVID-19.

RESUMO
As reações emocionais têm impacto sobre a saúde e a qualidade de vida das pessoas. Com o advento da neurociência nos anos 90, muitas pesquisas se concentraram na relação entre os circuitos neurais e as reações emocionais. Neste sentido, identificamos um crescimento de 2031% na pesquisa ligando emoções e saúde entre 1990 e 2022. Usando a ferramenta de mineração de texto chamada "Ferramentas Biotexto", realizamos uma pesquisa bibliográfica, focando as doenças da velhice e covid-19. Moléculas emocionais (EMs), produzidas pelo sistema endócrino, impactam a homeostase do corpo, afetando o equilíbrio biológico do corpo. Relacionamos os EMs com doenças dos idosos e da Covid-19, a fim de analisar o impacto dos estados emocionais no desenvolvimento e tratamento destas patologias. Para este fim, foi analisada a relação bidirecional entre ansiedade, depressão, doença cardíaca, derrame e doenças de Alzheimer e Parkinson. Finalmente, a gravidade do Coronavirus e os níveis de mortalidade foram relacionados aos níveis de cortisol, testosterona e serotonina.

Palavras-chave: emoção, saúde, doenças, moléculas, endocrinológicos, idosos, COVID-19.

1 INTRODUCTION

Human emotions are a growing topic in the scientific field. With the advent of neuroscience, in the 90's, many researches focused on the construction of the relationship between neural circuits and emotional reactions. This growth has broadened the knowledge about the area. Studying emotions is understanding their concepts, stimuli and implications. Emotional reactions impact people's general health and quality of life.

We carried out a literature survey, using text mining methods, and presented the relationship between emotions and health. We demonstrate how an emotional state can affect and be affected by the body's homeostasis. Identifying emotions, their causes, and their implications can help people's quality of life. The focus of the research is to establish a relationship between emotion and the main diseases of the elderly and Covid-19.

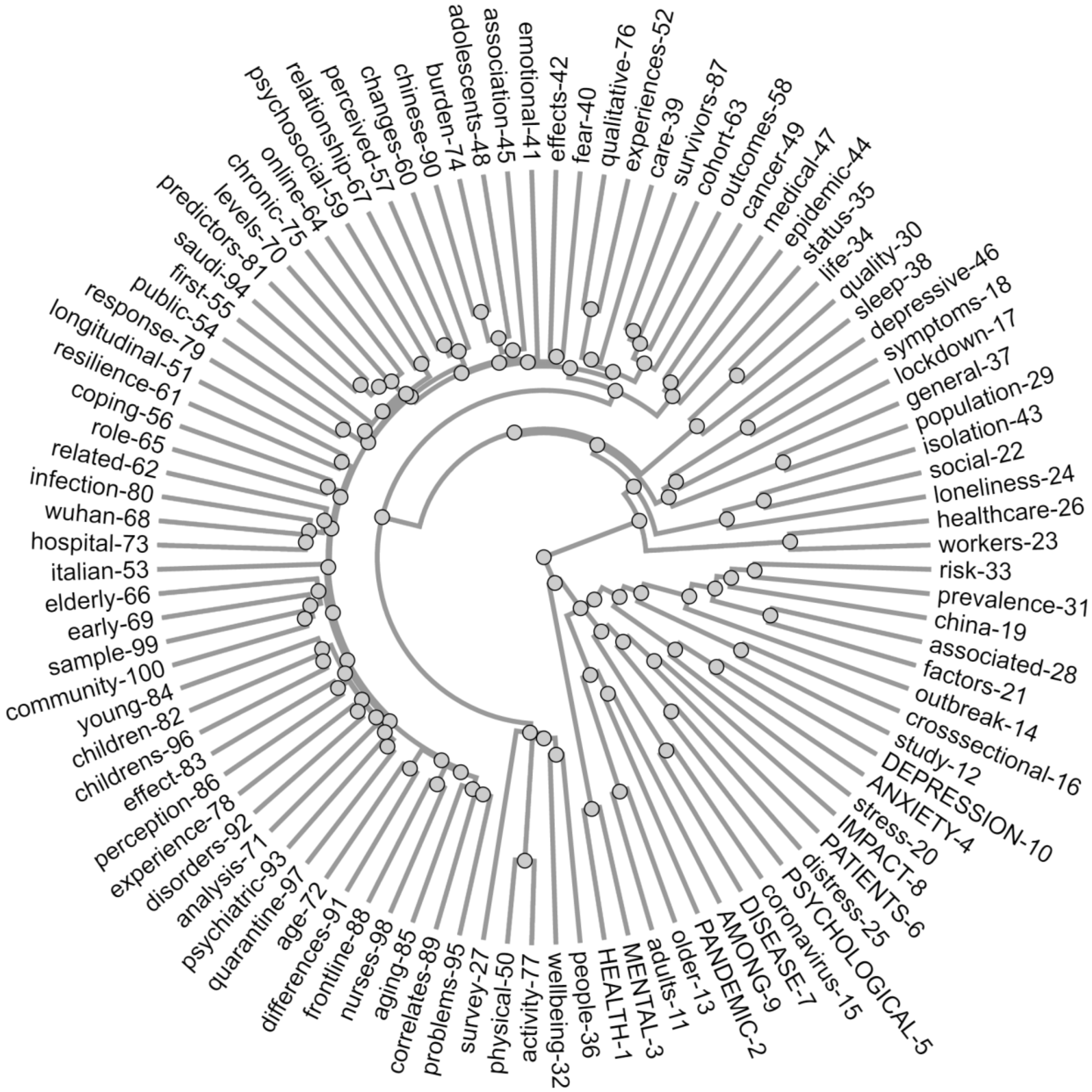
2 METHODOLOGY

We began our research by defining our literature inclusion criteŕios as follows:

1. **Keywords:** health, diseases, emotions, covid, elderly, cortisol, adrenaline, oxytocin, dopamine, testosterone, vasopressin;
2. **Scope:** Relationship between emotions and health, emotions and diseases in old age, and emotions and covid-19;
3. **Time period:** January 2012 to October 2022.

Next, we performed a literature review using the text mining tool "Biotext Tools" (MACHADO, D et al., 2021). We provided as search parameters the keywords "emotion health elderly covid" for the biotext tool.

Figure 1: Cluster tree generated with the result of the search performed in Biotext Tools.



Then we searched for articles that relate Covid-19 and the diseases of the elderly to the molecules produced by the endocrine system: cortisol, adrenaline, serotonin, oxytocin, vasopressin, dopamine, and testosterone. The search was conducted in PubMed, relating the words "diseases" and "elderly" to each of the emotion molecules cited, resulting in the terms: "diseases elderly cortisol", "diseases elderly adrenaline", "diseases elderly serotonin", "diseases elderly oxytocin", "diseases elderly vasopressin", "diseases elderly dopamine" and "diseases elderly testosterone".

3 THE SCIENCE OF EMOTIONS AND ITS RELATIONSHIP TO HEALTH AND DISEASE

The word emotion comes from the Latin word "*emovere, emotum*" which means movement toward the outside. Emotion is an experience common to humans and animals. This emotional experience of the individual can be perceived through emotional expressions and allows emotions to be classified. Among the classification models of human emotions, the best known is proposed by psychologist Paul Ekman (1992), with the concept of basic emotions defined as: happiness, surprise, fear, sadness, anger, and disgust (MEFTAH, Imen Tayari; LE THANH, Nhan; AMAR, Chokri Ben, 2010; DE VERE, Amber J.; KUCZAJ, Stan A.,2016;DE VERE, Amber J.; KUCZAJ, Stan A.,2016; Ekman,1992).

Basic emotions are identified through emotional responses resulting from external and internal stimuli. A stimulus is a signal perceived by the brain that triggers behavioral and physiological reactions. These stimuli provide the experience of emotion and connect the brain and the body through the release of chemicals called emotion molecules (EMs) (SUN, Lihua; PERÄKYLÄ, Jari; HARTIKAINEN, Kaisa M,2017; Pace-Schott EF et al.,2019; D'Hondt, et al, 2010; Pert, 1997).

EMs are classified into neurotransmitters, steroids, and peptides. Neurotransmitters are small molecules that generally carry information between neurons. Steroids are cholesterol-derived hormones released into the blood by endocrine glands and act at distant target sites. Peptides are small proteins made up of chains of amino acids that play a variety of roles in different types of cells in the body, including information transport (Pert, 1997; BALTHAZART, Jacques; BALL, Gregory F.,2006; HORTA, 2012, p. 49; HE, Matthew X.; HU, Z. B.,2017).

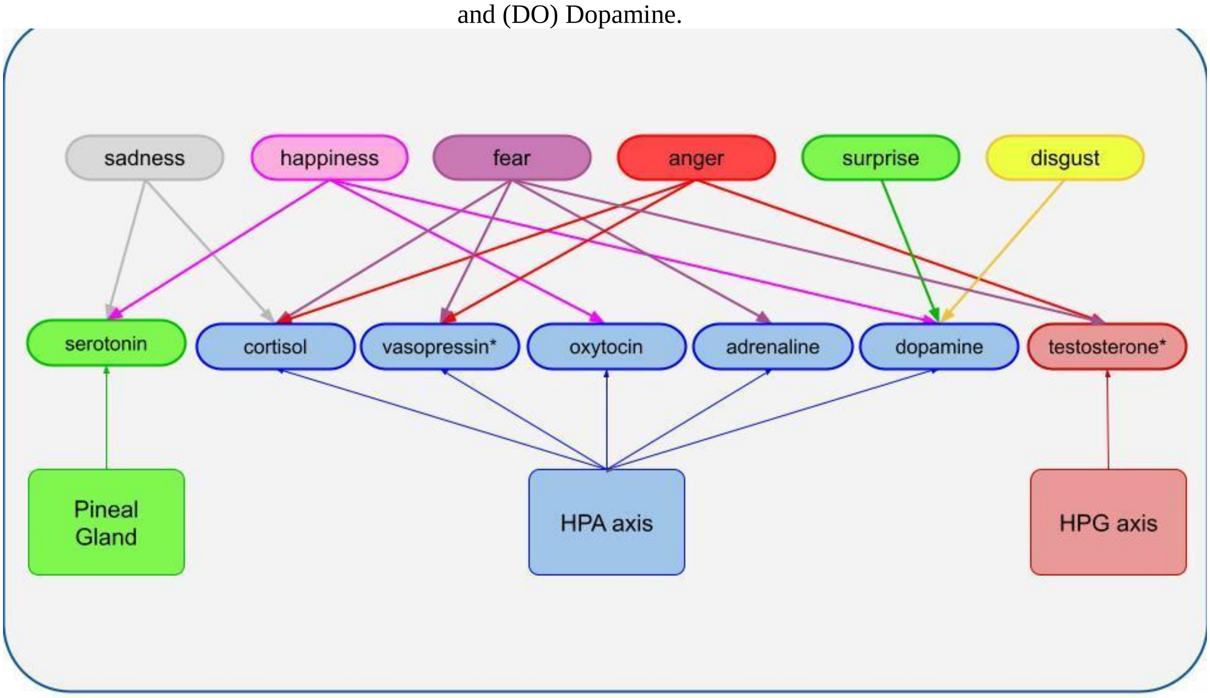
The human body is a communication network where balance, called homeostasis, promotes health and imbalance leads to disease. The EMs perform a broad role in regulating the organism, with the greatest impact on the communication network between the nervous, neuroendocrine, and immune systems (Pert,1997; LARSON, James S.,1999;WILLING, Ben et al.,2009; CACIOPPO, John T.; BERNTSON, Gary G,2011; DE WINDT, L. J. et al., 2002).

In our analyses we focus on the EMs produced by the endocrine glands. The endocrine system is a set of organs that share the coproduction of polypeptides, steroids and amino acid derivatives in order to act on distant target cells after binding to the receptor (CSABA, G.,2011; MAYER, Matthew L.; HANCOCK, Robert EW,2010; LA

PERLE, Krista MD.,2021; THYAGARAJAN, Srinivasan; PRIYANKA, Hannah P.,2012; Rachdaoui, N. e Sarkar, D. K., 2017).

Figure 2 shows the six basic emotions related to the main MS produced by the endocrine system.

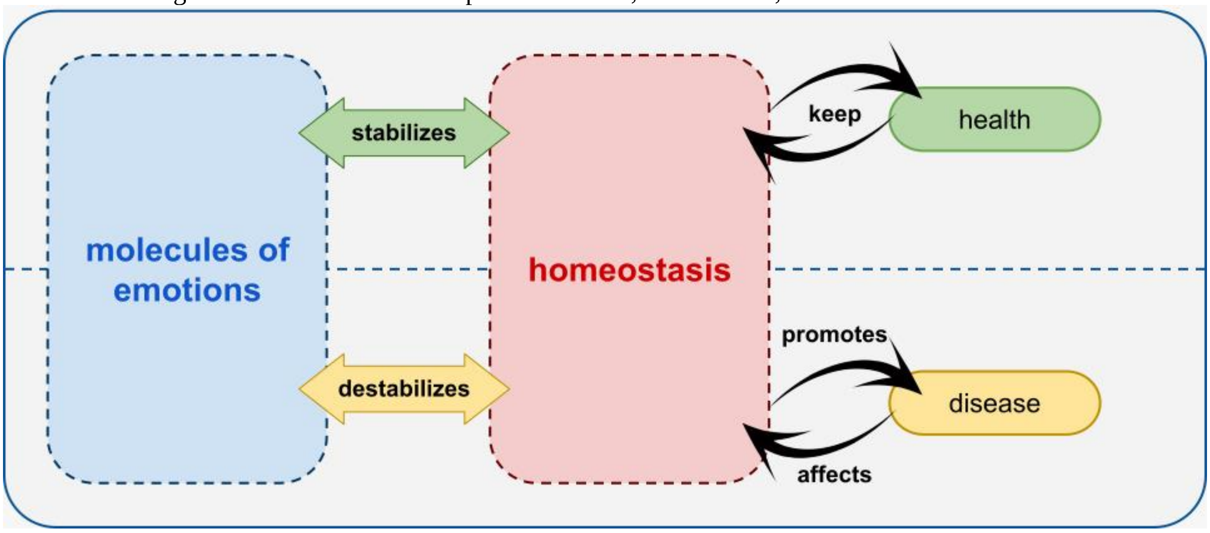
Figure 2: Relationship between basic emotions, EMs, and endocrine glands. The acronyms represent: (SE) Serotonin, (CO) Cortisol, (VP) Vasopressin, (OX) Oxytocin, (TE) Testosterone, (AD) Adrenaline and (DO) Dopamine.



Analyzing the relationship between the six basic emotions and EMs, we found that: happiness and sadness, entirely opposite emotions, are related to serotonin; fear is connected to cortisol, vasopressin, adrenalin, and testosterone; anger is related to cortisol; and disgust and surprise are connected only to dopamine. Among them, we highlight testosterone and vasopressin, substances little associated with emotions, but that influence anger and fear reactions. We present, in table 1, available in the supplementary material, details about the relationship of each emotion molecule with their respective basic emotions and emotional states and behaviors (PUTMAN, Peter LJ., 2006; COCCARO, Emil F., 2017; Bachner-Melman, Rachel, and Richard P. Ebstein, 2014;YANG, Hai-Peng et al, 2013).

The EMs can affect and be affected by homeostasis that is associated with states of health and disease (figure 3).

Figure 3: Bilateral relationship between EMs, homeostasis, health and disease.



Stability in the production of EMs assists in balancing the organism, maintaining health. Health, in turn, maintains the homeostasis that contributes to emotional stability. On the other hand, destabilization in the production of EMs can unbalance the organism, promoting diseases. Diseases affect the homeostasis that provides emotional destabilization. Thus, the analysis of the bilateral relationship between emotions and health is related to the analysis of the bidirectionality between emotions and diseases.

4 RELATIONSHIP BETWEEN EMOTION MOLECULES (EMS) AND DISEASE

Every illness, if not psychosomatic in foundation, has a psychosomatic component. The term psychosomatic comes from the joining of the Greek words "*psyche*" (mind) and "*soma*" (body). In this way, psychosomatics studies the relationship between mental states and physiological responses. Mental states affect the organs of the body through the connection of three interrelated components: neural, hormonal, and immunological (Pert,1997; NISAR, Hifsa; SRIVASTAVA, Rahul., 2018).

The EMs have different functions in the immune system. Dopamine and serotonin act in the interaction of the nervous and immune systems. Cortisol and oxytocin regulate the same systems. Testosterone, in turn, impacts on the suppression of the immune system. Table 2, available in the supplementary material, shows the relationship between EMs and the immune system, demonstrating the action of each one of them (CLOW, Angela; HUCKLEBRIDGE, Frank; THORN, Lisa, 2010; LI, Tong et al.,2017;LEACH, Sarah; SUZUKI, Kazuhiro., 2020; SHARMA, Drashya; FARRAR, J. David.,2020; SARKAR, Chandrani et al., 2010; LI, Mingan et al.,2022; MÖSSNER, Rainald; LESCH, Klaus-Peter, 1998; BAGANZ, Nicole L.; BLAKELY, Randy D.,2013;RUSSELL, James

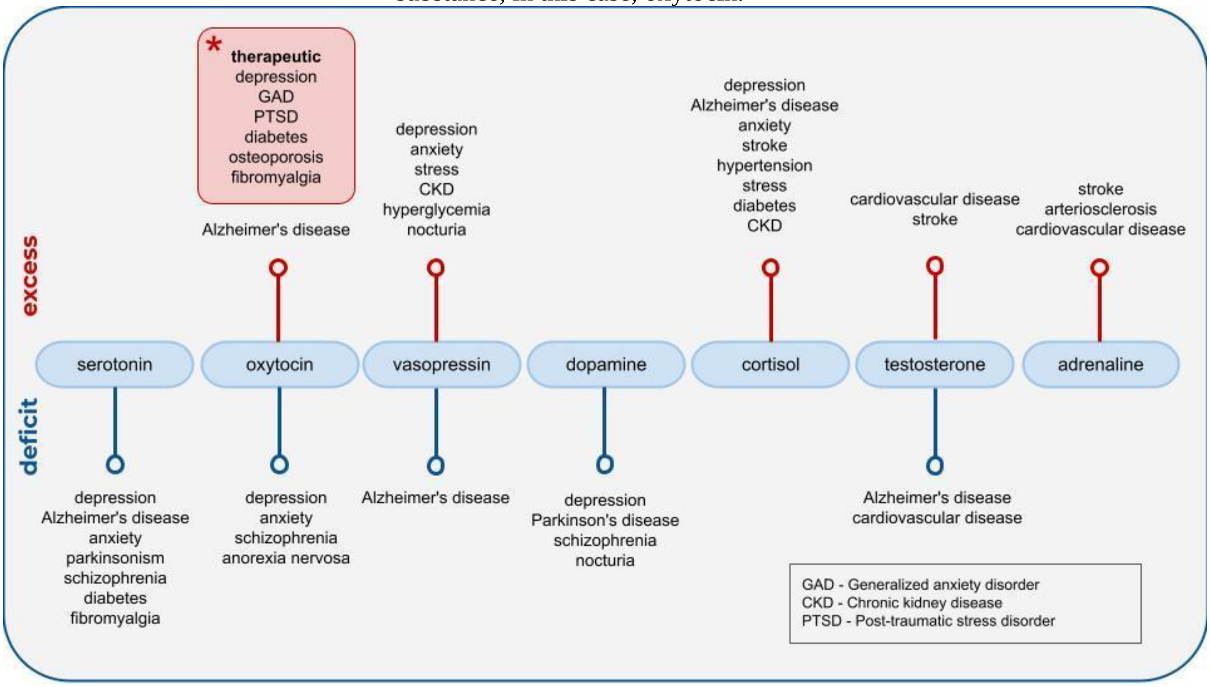
A.; WALLEY, Keith R.,2010;JESSOP, D. S. et al.,1995; PIRHADI, Roxanna et al., 2020).

The interaction, direct or indirect, of EMs in the suppression or stimulation of the immune system allows us to establish a relationship between the product of emotional responses to various pathologies or treatment of diseases. Cortisol, for example, when secreted in large quantities, leads to a pathological response associated with various heart diseases. Oxytocin, on the other hand, has been indicated in the treatment of fibromyalgia and schizophrenia (Vogelzangs, Nicole, Aartjan TF Beekman, Yuri Milaneschi, Stefania Bandinelli, Luigi Ferrucci, and Brenda WJH Penninx.,2010; MAMELI, S. et al.,2014;SUN, Jeehae et al.,2016).

Diseases can also have a reflection on the emotions. There are, for example, studies on the occurrence of anxiety and depression in people diagnosed with cancer, cardiovascular diseases, stroke, and Alzheimer's and Parkinson's diseases (Spiegel, David,1996; Massie, Mary Jane,2004; Olin, Jason T., Ira R. Katz, Barnett S. Meyers, Lon S. Schneider, and Barry D. Lebowitz, 2002; NICCOLINI, Flavia.,2015; Gaete, Jorge Moncayo, and Julien Bogousslavsky, 2008, AZEVEDO IM et al.,2017).

Figure 4 presents the relationship between EMs and diseases, with a focus on the pathologies associated with old age. We sought to identify the biological consequences of the excess or scarcity of these substances. In tables 3 and 4, of the supplementary material, we provide the effect of excess or scarcity of the EMs and their association with diseases in general and with the diseases of the elderly, respectively.

Figure 4: The relationship between the EMs produced by the endocrine system and the associated diseases. The diseases highlighted in the (*) indicate the possibility of the therapeutic use of the related substance, in this case, oxytocin.



As represented in figure 4, we see that the imbalance in the synthesis of EMs The excessive production of cortisol and vasopressin leads to 9 and 6 pathologies, respectively. While deficits in serotonin and dopamine lead to another 7 and 6 diseases, respectively.

5 THE BIDIRECTIONAL RELATIONSHIP BETWEEN OLD AGE DISEASES AND EMOTIONS

Aging is characterized by numerous changes that occur at different levels of the biological hierarchy. Biological mechanisms underlying aging are central to increased susceptibility to disease. Oxidative damage constitutes one of the mechanisms for increased disease in aging, which can lead to imperfect folding in protein structure, mutations, and a host of other harms (DA COSTA, João Pinto et al., 2016; Ferrucci, 2020; COMBES, Guillaume F.; PELLAY, François-Xavier; RADMAN, Miroslav, 2020).

Stress is a state of emotional arousal that contributes to oxidative damage. Oxidative stress is defined as an imbalance between oxidants and antioxidants, with oxidants predominating. While organic balance is preserved in homeostasis, in oxidative stress a radically altered new steady state occurs. This new state of imbalance promotes the emergence of diseases, such as hypertension, cardiovascular diseases, and diabetes (SIES, Helmut, 1997; URSINI, Fulvio; MAIORINO, Matilde; FORMAN, Henry Jay, 2016; PAPACONSTANTINOU, John,2019; KĘDZIORA-KORNATOWSKA, Kornelia et al.,2009).

Among the diseases of aging, we highlight: cardiovascular diseases, hypertension, atherosclerosis, diabetes, hyperthyroidism, musculoskeletal disorders, rheumatoid arthritis, osteoarthritis, polymyalgia rheumatica, temporal arteritis, osteoporosis, Paget's bone disease, falls, dementia (Alzheimer's and Parkinson's diseases) and emotional diseases (anxiety and depression) (RUMSEY, KARLA E., 1988;BRYANT, Christina;JACKSON, Henry; AMES, David, 2008;ZHANG, Yaxin; CHEN, Yujing; MA, Lina., 2018;SOSA-ORTIZ, Ana Luisa; ACOSTA-CASTILLO, Isaac; PRINCE, Martin J.,2012).

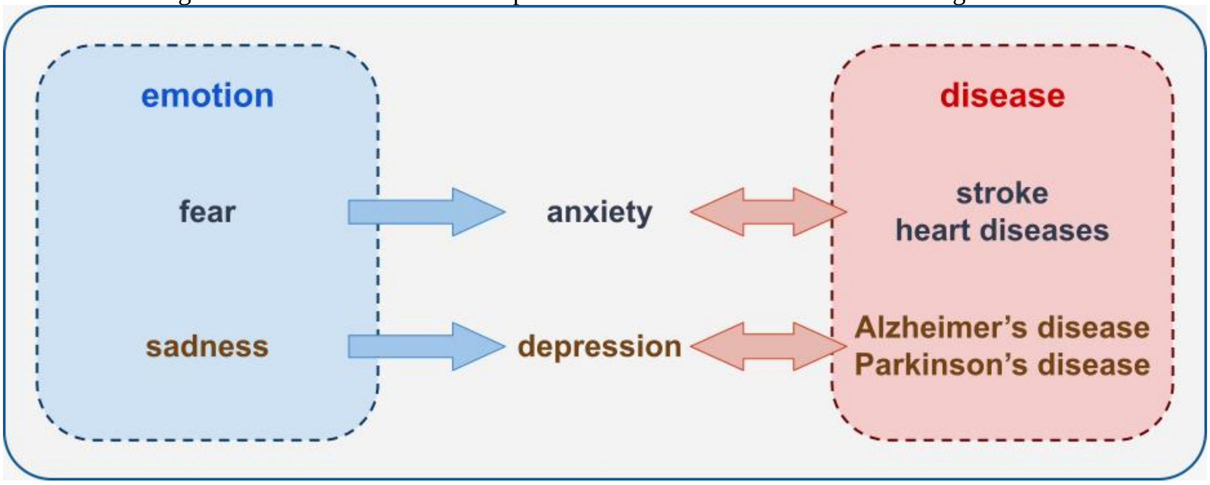
In order to constitute the bidirectional relationship between old age diseases and emotions, we related the two main emotional diseases, anxiety and depression, with cardiovascular diseases, stroke, and Alzheimer's and Parkinson's diseases. To do this, we surveyed the impact of anxiety and depression on old age (figure 5).

A study on anxiety in the elderly revealed that the prevalence of this disorder in late life ranges from 1.2% to 15% in community samples and from 1% to 28% in medical settings. Recent data relate anxiety among the elderly to increased morbidity and mortality, especially related to cardiovascular and brain diseases, such as stroke (BRYANT, Christina;JACKSON, Henry; AMES, David, 2008;VAN BALKOM, Anton JLM et al., 2000; CAIRNEY, John et al., 2008;DONOVAN, Nancy J. et al., 2018; KRELL-ROESCH, Janina et al., 2018;PÉREZ-PIÑAR, María et al.,2017).

Geriatric depression is becoming a major public health problem. Its effect on health increases when in comorbidity with a chronic medical condition. Alzheimer's and Parkinson's diseases are accompanied by a high incidence of depression and can affect the treatment and prognosis of these pathologies (ZHANG, Yaxin; CHEN, Yujing; MA, Lina., 2018; MDAWAR, Bernadette; GHOSSOUB, Elias; KHOURY, Rita.,2020; POLITIS, Marios; NICCOLINI, Flavia., 2015, LAVELLI B. C., et al., 2022).

Figure 5 shows the bidirectional relationship between emotions, anxiety, depression, cardiovascular disease, stroke, and Alzheimer's and Parkinson's diseases.

Figure 5: bidirectional relationship between emotions and diseases in old age.



The state of fear can lead to the development of anxiety which correlates with cardiovascular disease and stroke. Sadness, in turn, can lead to depression, which connects with Alzheimer's and Parkinson's diseases. By identifying these connections, we can see the bidirectionality present between them (LI, Jian; HUANG, Jin-Song., 2020; MOUCHET-MAGES, Sabine; BAYLÉ, Franck J., 2022).

Checking the bidirectional relationship between anxiety and cardiovascular diseases, we identified that anxiety causes heart rate variability, which can cause heart failure, arrhythmia, and provide coronary heart disease. While patients with a history of heart disease, such as myocardial infarction and arrhythmia, may develop anxiety (OUAKININ, Silvia Raquel Soares., 2016; EMDIN, Connor A. et al.,2016; BATELAAN, Neeltje M. et al.,2016;SANTOS, João Manoel Theotonio dos, 2028; ABURUZ, Mohannad Eid; MASA'DEH, Rami., 2017; MIKHAYLOV, Alexey Y.; YUMASHEV, Alexei V.; KOLPAK, Eugeny.,2022).

Anxiety, especially phobic anxiety, is a risk factor for stroke. In turn, stroke can provide the development of anxiety. In such cases, there are chances of the disease becoming disabling, increasing dependency, morbidity, and even the possibility of mortality. This factor is relevant to the extent that approximately 20% of stroke patients experience significant levels of anxiety at some point after the disease (PÉREZ-PIÑAR, María et al.,2017; EMDIN, Connor A. et al.,2016; KIM, Yong-Ku,Ed., 2020;CHUN, Ho-Yan Yvonne et al., 2018; BRYANT, Christina;JACKSON, Henry; AMES, David, 2008; KNAPP, Peter et al.,2017).

Alzheimer's disease can cause depression in the same way that late-life depression can cause neurodegeneration becoming a risk factor for the development of Alzheimer's disease (LIU, Rong-Yu et al., 2000; MDAWAR, Bernadette; GHOSSOUB, Elias; KHOURY, Rita.,2020).

Patients with Parkinson's disease have a high risk of developing depression because of the possible metabolic reduction of serotonin. Depressed patients also have a higher risk of developing Parkinson's disease (POLITIS, Marios; NICCOLINI, Flavia.,2015; SHEN, Cheng-Che et al.,2013).

6 RELATIONSHIP BETWEEN COVID AND EMOTIONS

Covid-19 is a disease caused by the coronavirus that causes acute infection in the respiratory tract. Designated as Severe Acute Respiratory Syndrome Coronavirus-2 (Sars-Cov-2), it was responsible for the pandemic declared on March 11, 2020 (FREITAS, André Ricardo Ribas; NAPIMOGA, Marcelo; DONALISIO, Maria Rita, 2020; BOMFIM, José Henrique Gialongo Gonçales; DA SILVEIRA GONÇALVES, Juliana, 2020; DE ALMEIDA HAMMERSCHMIDT, Karina Silveira; SANTANA, Rosimere Ferreira,2020).

Studies have linked the implications of emotional states and EMs on covid-19 and vice versa (Figure 6). There is, for example, research linking high cortisol levels to Coronavirus mortality, just as there are studies on increased anxiety and depression during the pandemic. LAKHAN, Ram; AGRAWAL, Amit and SHARMA, Manoj (2020), report up to a 35% increase in cases of anxiety and 20% increase in depression in a combined study population of 113,285 individuals (TAN, Tricia et al., 2020).

Relating the EMs to covid-19, we obtained the results shown in figure 6.

Figure 6: PubMed search result with the terms: covid cortisol, covid testosterone, covid serotonin, covid dopamine, covid adrenaline, covid oxytocin, and covid vasopressin.

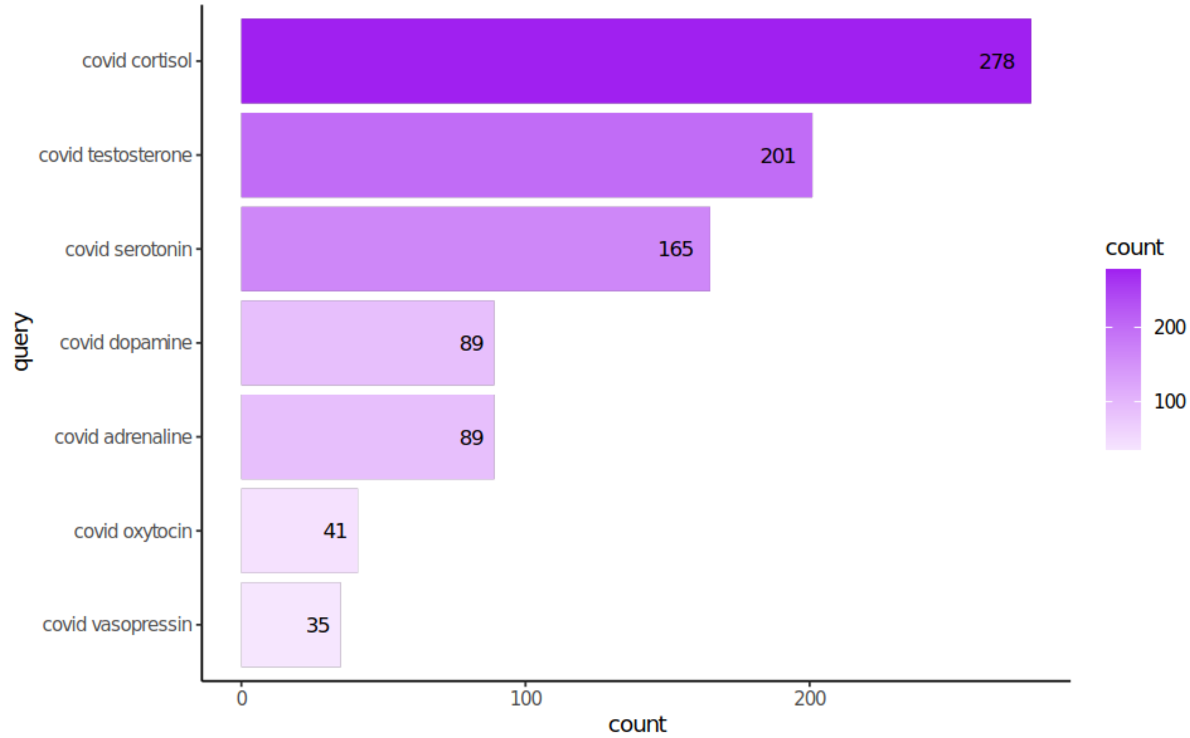
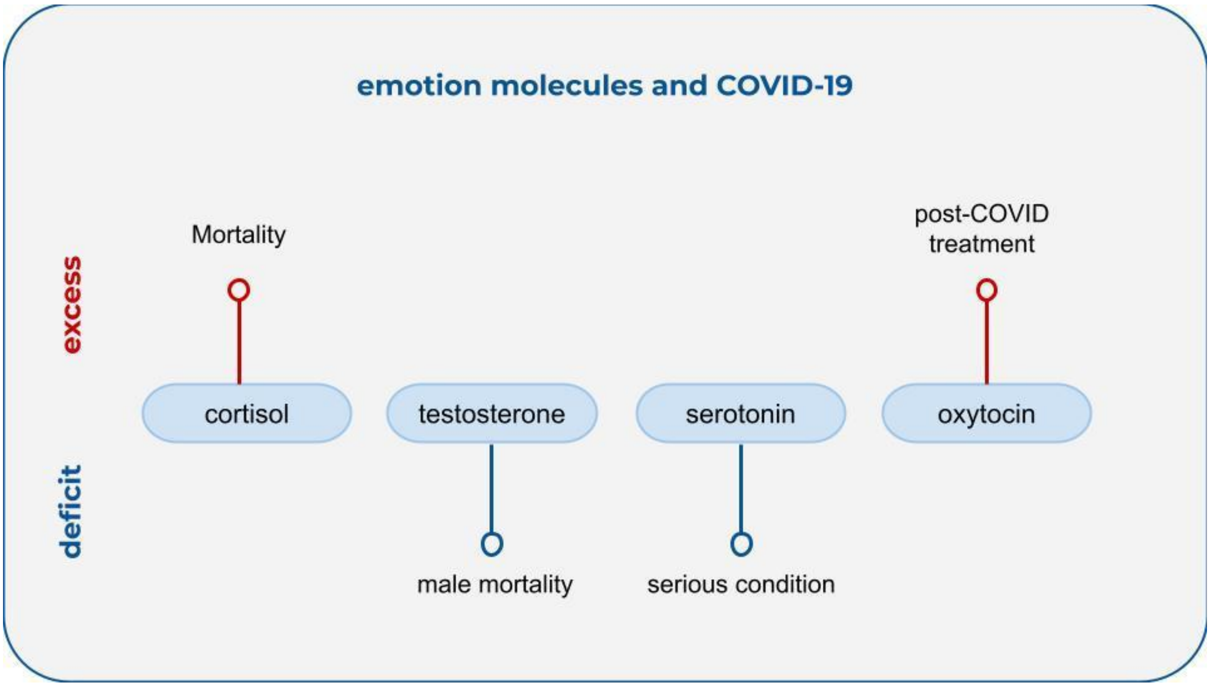


Figure 6 reveals the number of articles related to MS. We chose for the analyses the three largest results: cortisol (278), testosterone (201) and serotonin (165). In addition to these substances, we also evaluated oxytocin (41).

We present, in figure 7, the relationship of EMs and covid-19. We first look at the excess or lack of these substances and how this may impact on Coronavirus severity and mortality rates. We then explore the therapeutic potential of oxytocin in the treatment of post-covid-19.

Figure 7: relationship between emotion molecules (cortisol, testosterone, serotonin and oxytocin) and covid-19.



Cortisol has the largest number of studies, with a total of 278 articles. Its relationship with Covid-19 may be linked to two factors: pneumonia and depression. Elevated cortisol is an independent biomarker that provides adverse prognosis and mortality in patients with pneumonia. In the case of depression, high cortisol levels are associated with mortality rates in depressed persons hospitalized for the illness (FARIAS, Lucas de Pádua Gomes de; STRABELLI, Daniel Giunchetti; SAWAMURA, Márcio Valente Yamada,2020; PAL, Rimesh; BANERJEE, Mainak; BHADADA, Sanjay K.,2020; HERBERT, J.,2013; RAMEZANI, Mahtab et al., 2020).

Second in study volume, with 201 articles, is testosterone. The relationship between testosterone and covid-19 in the male population is controversial. Some studies claim that low testosterone may serve as a protective factor against Coronavirus infection for men in certain situations. However, a growing body of research states otherwise, presenting evidence that low testosterone levels are associated with increased severity and mortality from Covid-19 in male patients (YASSIN, Aksam et al.,2022; LANSER, Lukas et al.,2021).

Serotonin ranked third with 165 articles. JI, Pan et al. (2020) surveyed patients with covid-19 and revealed that those who progressed to the severe stage of the disease had elevated markers of inflammation. Inflammation reduces serotonin levels in the body, which in turn favor a pro-inflammatory state. Thus, there are studies suggesting the use of serotonin reuptake inhibitors as a therapeutic strategy for Covid-19 (JI, Pan et al. , 2020; PASHAEI, Yaser, 2021).

Oxytocin presented a total of 41 articles related to covid-19. During Coronavirus infection, there is an interruption of the function of the immune and neuroendocrine system which can promote oxytocin dysfunction. This dysfunction can lead to autoimmune disease. Oxytocin is known for its anti-inflammatory, antioxidant, and immunomodulatory effects. Its replacement can help shut down an overactive immune system (SIRIGU, Angela; DIEP, Phuoc-Tan; DE KOK, Véronique., 2022;THAKUR, Pratibha; SHRIVASTAVA, Renu; SHRIVASTAVA, Vinoy K.,2021;SOUMIER, Amélie, 2020;CALDERONE, Alba et al.,2020).

7 CONCLUSION

Our study indicated a 2031% increase in research posted on PubMed, between 1990 and 2022, relating emotions and health. From 931 published articles in 1990, the volume of research jumped to 19,843 in September 2022. To substantiate the association between emotions and health, we analyzed the bidirectional relationship between emotions and diseases, with a focus on diseases of old age and covid-19.

By examining the relationship between emotions and diseases in old age, we identify the role of hormones such as cortisol, testosterone, and oxytocin in the prevention, expression, aggravation, and treatment of these diseases.

Excess cortisol, known as the stress hormone (SADOUL, Bastien; GEFFROY, Benjamin.,2019) impacts diseases such as anxiety, depression, cardiovascular disease, diabetes, hypertension, Alzheimer's, stroke, stress, and chronic kidney disease. These 9 diseases account for half of the analyzed diseases related to seniors, that is, cortisol acts negatively on 50% of them.

The role of testosterone in cardiovascular disease is still undefined. There are studies that support a beneficial effect of testosterone replacement therapy in reducing mortality, while other reports suggest that testosterone may increase the risk of serious cardiovascular events (GAGLIANO-JUCÁ, Thiago; BASARIA, Shehzad.,219).

Oxytocin has therapeutic potential in several diseases of the elderly. Among the 18 diseases studied, the therapeutic potential of oxytocin was signaled in 6 of them.

Analyzing the relationship between emotions and covid-19, we identified that increased cortisol, testosterone, and serotonin have been related to disease severity.

Oxytocin, in turn, may aid in the treatment of autoimmune diseases developed after coronavirus infection.

We conclude that many diseases of old age and covid-19 can be affected or affect EMs. We believe that the major diseases of old age and severity by covid-19 can be avoided or treated with a more emotionally balanced life. Thus, the bilateral relationship between emotion and health should also be thought of from the bilateral relationship between emotions and diseases, integrating the data analyzed during a diagnostic process. An emotional anamnesis can help in the identification and prevention of diseases. Therefore, we suggest a greater use of emotions in medicine and technology.

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SUPPLEMENTARY MATERIAL

Table 1

Gland	Molecule	Reactions and associated emotional states	Emotions	Papers
Hypothalamus	Dopamine	Positive and negative mood;	Disgust and surprise	BODIS, J. et al.,1992; DFARHUD, Dariush; MALMIR, Maryam; KHANAHMADI, Mohammad,2014
Pineal	Serotonin	Joy and recognition of negative moods, depression, anxiety	Happiness and Sadness	BODIS, J. et al.,1992;(DFARHUD, Dariush; MALMIR, Maryam; KHANAHMADI, Mohammad,2014; HENSLER, Julie G.,2010;COWEN, Philip J.; BROWNING, Michael.,2015;AKIMOVA, Elena; LANZENBERGER, Rupert; KASPER, Siegfried.,2009;
Hypophysis	oxytocin	Affective connection, well-being, and stress reduction	Happiness	YANG, Hai-Peng et al,2013;SHIMA, Rei; YOSHIOKA, Tohru,2019
Hypophysis	Vasopressin	Aggression, anxiety, stress;	Fear and anger	YANG, Hai-Peng et al,2013;ZINK, Caroline F. et al.2010;BELOKOSKOVA, Svetlana G.; TSIKUNOV, Sergey G.,2018
Adrenal	Adrenaline	Anxiety, depression, pain, fear memory	Fear	RAO, Yi. ,2019;KIANI, Aysha Karim et al.,2020;ZHU, Xiangjia et al.,2021;OLIVEIRA, Ana et al.,2018;
Adrenal	Cortisol	Depression, anxiety, stress	Fear and anger	RODRIGUEZ, Angela C.,2015; Aysha Karim et al.,2020;ZHU, Xiangjia et al.,2021;BURKE, Heather M. et al.,2005;ELNAZER, Hesham Yousry; BALDWIN, David

				S.,2014;HELLHAMMER, Dirk H.; WÜST, Stefan; KUDIELKA, Brigitte M.,2009.
Gonads	Testosterone	Aggression, self-confidence	Fear and anger	JANOWSKY, Jeri S.,2006;GENIOLE, S. N. et al.,2020;DALTON, Patricio S.; GHOSAL, Sayantan,2014;

Table 1: Relationship between the glands of the endocrine system and the molecules of the emotions. The link to the respective emotions and their impact on emotional and behavioral states.

Tabela 2

Emotion of molecule	Acting on the immune system	Papers
Cortisol	Contra regulates the balance of substances important in promoting and inhibiting the immune system.	CLOW, Angela; HUCKLEBRIDGE, Frank; THORN, Lisa (2010).
Oxytocin	It regulates the body's defense system by activating its receptors in central immune organs, tissues, and peripheral immune cells.	LI, Tong et al. (2017).
Adrenaline	It influences the immune function, acting in the regulation of the immune system, locally and systematically.	LEACH, Sarah; SUZUKI, Kazuhiro. (2020);SHARMA, Drashya; FARRAR, J. David.,2020.
Dopamine	It creates a bridge between the nervous and immune systems, acting on the regulation mechanism of the immune system.	SARKAR, Chandrani et al. (2010);LI, Mingan et al. (2022)
Serotonin	It performs an interaction between the central nervous and immune systems.	MÖSSNER, Rainald; LESCH, Klaus-Peter,(1998);(BAGANZ, Nicole L.; BLAKELY, Randy D.(2013).
Vasopressin	It works on the alteration of cytokines, neuroimmunity, prostaglandins, humoral immunity, and immune cells. Provides information about the interaction between the endocrine and immune systems.	RUSSELL, James A.; WALLEY, Keith R.(2010);JESSOP, D. S. et al. Vasopressin is located within lymphocytes in the rat spleen. **Journal of neuroimmunology**, v. 56, n. 2, p. 219-223, 1995.
Testosterone	It acts as an immunosuppressant.	PIRHADI, Roxanna et al. (2020)

Table 2:Actions of emotion molecules on the immune system.

Table 3

Emotion of molecule	excess	Déficit	Therapeutic Use	Papers
Serotonin		Depression, epilepsy, anxiety, schizophrenia, Diabetes, Alzheimer, Parkinson, fibromyalgia		DFARHUD, Dariush; MALMIR, Maryam; KHANAHMADI, Mohammad,2014; PETRUCCI, Alexandra N. et al.2020;EL OUSSINI, Hajer et al.,2016;POURHAMZEH, Mahsa et al.2021;DORSZEWSKA, Jolanta et al.,2017;OH, Chang-Myung; PARK, Sangkyu; KIM, Hail.,2016;MDAWAR, Bernadette; GHOSSOUB, Elias; KHOURY, Rita.,2020;POLITIS, Marios; NICCOLINI, Flavia.,2015;SAMBORSKI, W. et al.,1996; HÄUSER, Winfried et al.2013.
Oxytocin		Anorexia nervosa, schizophrenia	Depression, anxiety disorder, post-traumatic stress disorder, diabetes, osteoporosis, fibromyalgia	MATSUSHITA, Hiroaki et al.,2019;ELABD, Seham; SABRY, Ismail.,2021;;BREUIL, Véronique; TROJANI, Marie-Charlotte; EZ-ZOUBIR, Amri.,2021;DING, C.; LEOW, MK-S.; MAGKOS, F.,2019;RASH, Joshua A.; AGUIRRE-CAMACHO, Aldo; CAMPBELL, Tavis S.,2014;BOLL, Sabrina et al.,2018;MAMELI, S. et al.,2014
Vasopressin	Anxiety, depression, acute stress, chronic	Alzheimer		BELOKOSKOVA, Svetlana G.; TSIKUNOV,

	kidney disease, hyperglycemia, metabolic syndrome, nocturia, stroke			Sergey G.,2018; LIU, Rong-Yu et al.,2000;ALBERT, Stewart G. et al. 1989;BANKIR, Lise; BOUBY, Nadine; RITZ, Eberhard.,2013;MCKEIGUE, Paul M.; REYNARD, John M.,2000;KARIO, Kazuomi; SHIMADA, Kazuyuki; PICKERING, Thomas G.,2003;
Cortisol	Anxiety, depression, cardiovascular disease, Diabetes, hypertension, Alzheimer's, stroke, stress, chronic kidney disease			ZHAO, Zi-Yan et al.,2003;WEINER, Myron F. et al. ,1997; OUANES, Sami; POPP, Julius.,2019;OLSSON, Tommy et al.,1992; GUSTAFSON, Yngve et al. ,1993;CARDOSO, Estela María del Luján et al.,2016;HELLHAMMER, Dirk H.; WÜST, Stefan; KUDIELKA, Brigitte M.,2009
Adrenaline	Cardiovascular disease; stroke, arteriosclerosis			FAKHRZADEH, H.; SHARIFI, F. ,2012;HAUSS, W. H.; BAUCH, H. J.; SCHULTE, H,1990;
Dopamine		Parkinson's Disease, Depression, schizophrenia, fibromyalgia		SEGURA-AGUILAR, Juan et al.,2014;TRIARHOU, Lazaros C.,2013;GRACE, Anthony A.,2016;WOOD, Patrick B. et al.,2007;WOOD, Patrick B. et al. ,2009;Carlsson, Arvid, and Maria L. Carlsson.,2022
Testosterone	Cardiovascular Disease, Stroke	Alzheimer's, cardiovascular disease		LV, Wenshan et al.,2016;OHLSSON, Claes et al. ,2011;SOISSON

				, Véronique et al.,2013;VIGEN, Rebecca et al. ,2013;

Table 3: The relationship between diseases and the excess or lack of emotion molecules in the body.
Oxytocin also has therapeutic potential.

Table 4

Disease	Neurotransmitters
Depression	Serotonin, oxytocin, vasopressin, dopamine, cortisol
Alzheimer's disease	Serotonin, Vasopressin, Cortisol, Testosterone
Anxiety	Serotonin, oxytocin, vasopressin, adrenalin, cortisol
Parkinson's disease	Serotonina,Dopamina
Osteoporosis	Oxytocin
Stroke	Vasopressin, adrenaline, cortisol, testosterone
Hypertension	cortisol
Stress	Oxytocin, cortisol
Disease cardiovascular	Cortisol, adrenaline
Schizophrenia	Serotonin, oxytocin, dopamine
Diabetes	Serotonin, oxytocin, cortisol
Epilepsy	Serotonin
Chronic kidney disease	Vasopressin, cortisol
Hyperglycemia	Vasopressin
Arteriosclerosis	Adrenaline
Nocturia	Vasopressin
Anorexia nervosa	Oxytocin
Fibromyalgia	Oxytocin, dopamine

Table 4:Relationship of emotion molecules to diseases in old age