

UNIVERSIDADE DA BEIRA INTERIOR Ciências Sociais e Humanas

# Neuropsychotherapy: a preliminary review

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Versão Definitiva Após Defesa Pública

## Dissertação para a obtenção do grau de Mestre em Psicologia Clínica e da Saúde

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Covilhã, Julho de 2019

## Acknowledgements

This section will be written both in English and in Portuguese.

First, I would like to thank Professor Luis Maia for challenging me to write my dissertation about the topic of neuropsychotherapy and for guiding me through this process. I would also like to thank my family, and mainly my parents and grandparents. Without their unconditional love and support, I would not be able to get through this. To my friends, especially to Paul Lima and Michael Köster for the linguistic aid, and to João Bernardo, Miguel Santos, and Fábio Monteiro, for the constant feedback with wisdom and good humor in equal parts. To Cláudia, for being there for me throughout the whole process. Her patience is unmatched. Finally, to Doctor Jorge Alves, for accepting to co-orientate this dissertation, and for being like a mentor to me during the last few months.

E agora, em português, porque a minha avó não compreende inglês.

Antes de mais, gostaria de agradecer ao Professor Doutor Luis Maia por me lançar o desafio de escrever a minha dissertação de mestrado sobre a neuropsicoterapia, e por me ter orientado durante todo o processo. Gostaria também de agradecer à minha família, mas principalmente aos meus pais e aos meus avós pelo amor e apoio incondicional que me dão, sem os quais nunca teria conseguido levar este processo a termo. Aos meus amigos, especialmente ao Paul Lima e ao Michael Köster pelo apoio com alguns termos técnicos em alemão, e ao João Bernardo, ao Miguel Santos e ao Fábio Monteiro, pelo suporte constante que tinha tanto de sabedoria como de bom humor. À Cláudia, por estar sempre comigo durante este processo. A paciência dela não tem igual. Finalmente, ao Doutor Jorge Alves, por ter aceite o convite para coorientar esta dissertação, e por ter sido como um mentor para mim ao longo destes últimos meses.

## Resumo

O termo neuropsicoterapia tem dois significados: a psicoterapia como ferramenta para a reabilitação neurológica (Ellis, 1989; Judd, 1999) e a psicoterapia informada pelas neurociências (Grawe, 2007). Sendo um conceito relativamente recente, ainda não existia nenhuma revisão da literatura com uma abordagem sistemática à pesquisa. Nesta dissertação pretende-se dar resposta a essa lacuna, sendo efetuada uma revisão da literatura com uma abordagem sistemática à pesquisa da literatura com uma abordagem sistemática à pesquisa. Nesta dissertação científicas (EBSCO, B-on, MEDLINE/PubMed, PsycINFO, Web of Science e Scielo). Oito artigos preencheram os critérios definidos para inclusão nesta revisão. Os artigos foram analisados cronológica, geográfica e tematicamente, tendo posteriormente sido discutidos os resultados.

## Palavras-chave

Neuropsicoterapia, psicoterapia, revisão da literatura, psicologia, neurociência

## Abstract

The term neuropsychotherapy has two distinct meanings: Psychotherapy as a tool for neurological rehabilitation (Ellis, 1989; Judd, 1999) and psychotherapy informed by neurosciences (Grawe, 2007). Being a relatively new concept, there was not any review of the literature with a systematic approach to article search yet (to the extent of our knowledge). This dissertation intends to fill that gap, by reviewing articles on the topic across six scientific databases (EBSCO, B-on, MEDLINE/PubMed, PsycINFO, Web of Science and Scielo). Eight articles fulfilled the inclusion criteria defined for this review. The existing literature is classified in chronological, geographical, and content-related terms. The dissertation ends with a discussion on the existing literature.

## Keywords

Neuropsychotherapy, psychotherapy, review of the literature, psychology, neuroscience

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## Acronyms

ADHD	Attention Deficit and Hyperactivity Disorder
APA	American Psychological Association
CAARS	Conners Adult ADHD Rating Scales
CNS	Central Nervous System
DMN	Default Mode Network
EMDR	Eye-Movement Desensitization and Reprocessing
fMRI	Functional Magnetic Resonance Imaging
MAP	Mindfulness Awareness Practice
PE	Psychoeducation
PTSD	Post-traumatic Stress Disorder
SQfMF	Self-Assessment Questionnaire for Mental Fatigue

### 1. Introduction

George Bush Sr., the former president of the United States of America, during his presidency, declared the decade of 90 as the decade of the brain. He made it so both by rising public investment in neuroscience investigation to unprecedented values for his time and by increasing the general awareness to this scientific field. In no moment in recorded history has there been this much interest in this area, which translates to both financial and scholarly efforts for the pursuit of knowledge and understanding of our nervous system, particularly in the central nervous system (CNS) structures (Jones & Mendell, 1999). This brought advances in the field that, among other things, allow us to understand that behavior, in all its forms and manifestations, origins in CNS activity. In turn, this points out the importance of a good neuroanatomic theoretical foundation, as well as a solid grasp in some of the basic principles of neural functioning in the understanding of human behavior (Kandel, Schwartz, Jessel, Siegelbaum & Hudspeth, 2013). This and the surging of new techniques for brain study (particularly, neural imaging techniques) gave us non-invasive access to aspects of neural structure and functioning, which might contribute to psychotherapeutic reasoning. Grawe (2007, p. 3) states that if all mental processes are grounded in neural processes, by analog logic changes in mental processes should be linked with significant changes in neural processes. LeDoux (2002) affirms that psychotherapy, being essentially a learning process, is a way to rewire the brain; therefore, psychotherapy uses biological mechanisms and neural underpinnings to treat patients with mental illnesses. Kandel and colleagues (2013) also defend this stance, and state that neuroimaging methods may be used not only in mental illness diagnosis but also in the assessment of the effectiveness of psychotherapy strategies and techniques.

In line with all that was referred above, psychology and neuroscience are becoming increasingly interconnected, as demonstrated by the creation of particular fields of research such as cognitive or affective neurosciences. Therefore, the number of publications that aim to explain or at least provide a correlation between concepts of both fields has grown during the last few decades. Consequently, psychotherapy has also followed this trend, and studies about the effect of the various psychotherapeutic approaches on the nervous system are being published daily, with an increasing rate (Goss, 2016).

### 2. Neuropsychotherapy

Some authors, influenced by this surge of studies on the neural basis of psychotherapy, have created several psychotherapeutic intervention models based on the contributions of neuroscientific knowledge to the understanding of human behavior. At first, these models were designed only taking in mind the psychotherapeutic intervention in neurological patients. Later, newer models were created aiming interventions with pathologies deemed of the psychiatric source. Eventually, all this effort led to the creation of a relatively new psychotherapy field: Neuropsychotherapy (Ellis, 1989; Grawe, 2007).

Neuropsychotherapy is a psychotherapeutic approach that can be defined as an approach to psychotherapeutic intervention that draws concepts, strategies, and techniques both from psychology and neuroscience; using neuroscientific knowledge and psychotherapy efficacy studies in order to maximize its efficacy (Grawe, 2007). The idea of having a neurologically informed psychotherapy can be retraced to Freud (1895, cit. in Walter, Berger & Schnell, 2009), however, due to the technological limitations of his time Freud eventually abandoned that idea in favor of the development of the psychoanalytic method (Kenny, 2016). Neuropsychotherapy currently follows two different major working definitions: psychotherapy as a neurological rehabilitation strategy (e.g. Ellis, 1989; Judd, 1999; Laaksonen & Ranta, 2013), and general psychotherapy informed by neuroscientific knowledge (e.g. Grawe, 2007; Walter, Berger & Schnell, 2009). Even though most literary sources usually establish a division between these definitions, both are based on the principle referred above, with the main difference being the population to which the intervention is aimed.

### 2.1. Neuropsychotherapy as a neurological rehabilitation strategy

Psychotherapy has been used as a rehabilitation strategy in neurologically impaired patients for about half a century, and its main function in this context is to ameliorate the cognitive, emotional and social problems that arise from the different types of neurological dysfunction (Judd, 1999; García-Molina, Roig-Rovira, Enseñat-Cantallops & Sánchez-Carrión, 2014). However, due to the lack of a core theoretical model, psychotherapeutic intervention for neurological rehabilitation outcomes have failed to produce significant positive outcomes (Laaksonen & Ranta, 2013). However, over the last twenty years there has been a conjoint effort between neuropsychologists to create an integrated approach, which is starting to bear fruits, showing promising results (Walter, Berger & Schnell, 2009; Laaksonen & Ranta, 2013). Neuropsychotherapy, as defined by Ellis (1989) and Judd (1999), requires a multidisciplinary approach to the rehabilitation of the said patients, drawing concepts from neurology, neurosciences, and psychology, and it varies in terms of procedure according to the different types of CNS disorders that the patients may experience (Laaksonen & Ranta, 2013).

As an example of a proposed core model, Warren and Judd (2019) affirm that one can take into account Suchy's (2011) model. Suchy, in an attempt to summarize emotional processing, created a model that includes five components, based on both psychological concepts and neuroanatomical knowledge: Reflexive reactions, triggered responses, emotional communication, emotional regulation, and emotional awareness.

Reflexive reactions include fight or flight responses, appetitive behaviors, arousal, and involuntary emotional expressions. This component is primarily mediated by the autonomic nervous system and endocrine systems (Suchy, 2011).

Triggered responses refer to fear, disgust, anger, and several forms of attraction. Sensory stimuli appear to have two main routes before being translated into a reaction: a "fast route", that goes through the thalamus and the primary sensory cortex, which enables a nearly immediate response; and a "slow route", which uses the secondary and tertiary sensory cortices and the hippocampus, allowing an evaluation of the stimulus content. Disruptions in this component may include overreactions, reduced reactions, and changes to the learning process (Suchy, 2011).

Emotional communication includes both emotional perception and emotional expression. The right cortical hemisphere is mainly responsible for emotional perception. Disruptions in the perceptual system may result in misinterpretation of the emotional content of non-verbal communication. Emotional expression involves frontal lobes and various subcortical structures. Disruptions in this system can cause symptoms that may lead to misinterpretation of the patient's emotional state, (e.g. aprosodia) (Suchy, 2011).

Emotional regulation mobilizes several different brain structures, such as the posterior cortex in the evaluation of situations and contexts and the frontal lobes and basal ganglia involved in initiating and inhibiting responses. Disruptions in this component may cause abulia, emotional lability and compulsive and/or addictive behavior (Suchy, 2011).

Emotional awareness refers to both self-awareness and awareness of others' emotions. The neuroanatomy of emotional awareness is not fully understood yet, but it involves many parts of the brain, such as the mirror-neuron system and the superior parietal cortex. The main concept associated with emotional awareness is empathy, which has cognitive and emotional components associated with portions of the dorsolateral prefrontal cortex. Anosognosia or alexithymia might be symptoms of disruptions in this system (Suchy, 2011).

Suchy's model is a prime illustrative example of a conceptual neuropsychotherapeutic model that correlates neural substrates and affected functions (Warren & Judd, 2019). However, a therapist must not limit itself to the damage caused directly by neural dysfunction and always take into account life reactions that the patients may experience in response to the event of neurologic injury (e.g. trauma, reactive depression). Furthermore, neurological patients are often subjected to discrimination due to their emotional and social impairments, which in turn may cause significant psychological suffering (Maffoni, Giardini, Pierobon, Ferrazzoli & Frazzitta, 2017). The psychotherapist working with neurological populations must consider all the referred factors in order to provide an adequate response and aid in the reintegration of

the patient, and it is in this aspect that neuropsychotherapy as a rehabilitation strategy differentiates itself from classic neuropsychological rehabilitation (Warren & Judd, 2019).

# 2.2. Neuropsychotherapy as a neurologically informed general psychotherapy

Neuropsychotherapy as a broader approach to psychotherapy (as opposed to the previous definition), is defined by being an approach that attempts to provide a theoretical foundation for psychotherapy based on validated and effective psychotherapeutic processes, as well as on neurological knowledge that may impact mental functioning (Grawe, 2007). Dahlitz (2015) further states that neuropsychotherapy is a neurobiologically informed framework that aims to view thought and behavior as a phenomenon emerging from motivational schemata developed for the goal of preserving or enhancing basic psychological needs.

Despite this more general definition, several conceptual core-models for neuropsychotherapy have been proposed, the most notable being Grawe's consistency-theoretical model (Grawe, 2007).

Grawe, drawing from Epstein's (1998) cognitive-experiential self-theory and Deci and Ryan's (2000) self-determination theory, developed a theoretical model of mental functioning that he coined as "consistency-theoretical model". In this model, Grawe took the four basic human psychological needs differentiated by Epstein (Orientation/control, pleasure/pain avoidance, attachment, self-esteem enhancement) and proposed that in order to satisfy and avoid violation of basic needs every individual develops motivational schemas. In turn, the individual's motivational schemas mainly direct his or her experience and behavior and guide the person throughout his or her life. These motivational schemas can be either of approach or avoidance nature, and depend on the person's developmental course (i.e. if the individual grows in an environment that fulfills his or her needs, his or her schemas will be mainly of an approach nature; if the environment is perceived as threatening the individual will develop mainly avoidance schemata).

By consistency, Grawe refers to "the agreement or compatibility of simultaneously transpiring neural/mental processes" (2007, p.168). Therefore, an organism's state can be considered "consistent" by Grawe's definition when there's no conflict between the different neural/mental processes, which is to say when the motivational schemas previously defined succeed in achieving the fulfillment of the individual's basic needs, and therefore, his or her goals, and do not conflict with each other.

Grawe also defined two main forms of inconsistency: discordance and incongruence. Discordance is defined as the incompatibility of simultaneously activated motivational schemas, and incongruence refers to when the experiences do not match the activated motivational goals (2007, p. 172).

Rossouw (2014, cit. in Kostyanaya, 2015), based on Grawe's model, developed an integrated model of neuropsychotherapy by introducing several new features and reinforcing some

previously used notions: Rossouw shifts the focus from motivational schemas to the importance of addressing the basic human needs when working with clients and introduces the need for safety as a primary need. According to Rossouw (2014, cit. in Kostyanaya, 2015), the need for safety is the key to the facilitation of neural proliferation, which translates into an increased approach motivational schemata and more adapted avoidance schemata; and compromised safety may cause neural protection and enhanced avoidance motivational schemata. Kostyanaya (2015) further states that in Rossouw's model the need for safety is activated through three of the needs identified by Grawe (orientation/control, pleasure/pain avoidance, and attachment). Rossouw's integrated theoretical model of neuropsychotherapy also differs from Grawe's by proposing that the concept of self and self-esteem is a higher order construct that results from neural patterns related to the primary needs and their interaction with the environment, may it be enriched or compromised. Therefore, in Rossouw's (2014, cit. in Kostyanaya, 2015) view, the self is a higher order construct which both strives to fulfill the basic needs and results from their culmination.

Ward, Delrue, and Plagnol (2017) also present a theoretical model in the light of neuropsychotherapy. According to the authors, it is possible to use cognitive notions of representation from neuroscience to explain how each person develops a cognitive internal world, designed as "representational space". This model is compatible with traditional notions of psychotherapeutic practices. For example, certain defense mechanisms, like denial or repression, may constrain the individual's representational space over time.

Using the example of post-traumatic stress disorder (PTSD), the authors use this model to explain several issues that have not been completely explored (Plagnol, 2004, cit. in Ward, Delrue & Plagnol, 2017). Those issues are the fact that in cases of trauma the memory of the traumatic event does not fade with time, as it tends to happen with other memories, and the fact that sometimes there is a delay between the event and the symptoms that trauma patients normally exhibit. Plagnol (2004, cit. in Ward, Delrue & Plagnol, 2017) states that all representation derives from sensory experience. The human being then codes the experiences via symbols and language, connecting them into the representational space. This, in turn, enriches the representational space, creating a deep, complex and rich personal internal world. The author also proposes that this internal world is relatively consistent over time. Similarly to Grawe's (2007) concept of incongruence, Plagnol (2004, cit. in Ward, Delrue & Plagnol, 2017) suggests that divergent fragments of the representational space, which may conflict with other codified experiences, may raise a degree of tension. Conway, Singer, and Tagini (2004) propose a similar view, with the concepts of self-defining memories and the Self-Memory system.

Following Ward, Delrue and Plagnol's (2017) view, traumatic events can, therefore, be seen as experiences that directly conflict with most of the other aspects of the self (notions about security, views about the self, etc.), and will raise the tension within the system. The memories associated with trauma will consequently stay active in its original, unprocessed form, and will not be integrated into the representational system. This leads to the "flashback" phenomenon and the repetitive intrusion of the memory.

To explain the previously mentioned issues of the trauma strengthening and delay through time, Ward, Delrue, and Plagnol (2017) suggest that the possibility of death or critical harm that often accompanies traumatic events forces the individual to face the perspective of death. This perspective and the concept of non-existing are alien to most of the people, conflicting with the majority of the ordinary fragments and notions that compose the average representational space. If any of those fragments or representations are active at the time of the flashback, the individual creates an association between the said representations and the traumatic event, therefore "contaminating" the original clean representation. Over time, conflict and incongruence infect increasingly more of the representational space, which explains both the strengthening phenomenon and the delay (Ward, Delrue & Plagnol, 2017).

Besides the referred models, Walter, Berger, and Schnell (2009) also proposed a working definition for neuropsychotherapy in Grawe's (2007) sense (i.e. psychotherapy referencing primarily neuroscientific evidence). In their perspective, the authors suggest a definition that encompasses and captures neuropsychotherapy as a field of applied research. According to the authors, the aim of neuropsychotherapy should consist in three separate, although interrelated, aspects: The identification of neural mediators and functional targets of psychotherapeutic effects, the determination of new therapeutic routes using neurotechnology, and the design of psychotherapeutic interventions based on neuroscientific knowledge (Walter, Berger & Schnell, 2009).

About the first aspect referred (the identification of neural mediators and functional targets of psychotherapeutic effects), the authors give the example of studies of basic learning mechanisms, specifically the fear conditioning and extinction in psychotherapy. Animal studies show that the extinction of conditioned fear responses happens due to active inhibition of amygdala reactions by the orbitofrontal cortex (Maren & Quirk, 2004). Fonzo et al. (2017) demonstrated that the inhibition of amygdala through the dorsolateral prefrontal cortex can be achieved with prolonged exposure therapy. This study shows several similarities with Maren and Quirk's (2004) animal studies and validates the applicability of the aforementioned aspect. About the second aspect (the determination of new therapeutic routes using neurotechnology), Walter, Berger, and Schnell (2009) refer as an example the use of neurofeedback as a direct route to functional targets, by the altering of psychopathological states using brain signals as feedbacks. Several studies explore the utility of functional magnetic resonance imaging (fMRI) in psychotherapy aiming several pathological symptoms, such as the relieving of obsessivecompulsive symptoms or drug-resistant hallucinations (DeCharms, 2008). However, Thybault, MacPherson, Lifshitz, Roth, and Raz (2018) recently conducted a systematic review about the effects of neurofeedback with fMRI, concluding that even though brain activity can be altered with fMRI neurofeedback, this does not necessarily translate into behavioral improvements.

Lastly, when addressing the third aspect (the design of psychotherapeutic techniques based on neuroscientific knowledge), Walter, Berger, and Schnell (2009) mention the use of eyemovement desensitization and reprocessing (EMDR) as a PTSD-oriented psychotherapeutic intervention. A recent systematic review (Novo Navarro et al., 2018) concluded that EMDR is indeed an effective, evidence-based technique for the treatment of PTSD, which validates the last aspect referred by Walter, Berger, and Schnell (2009) in their definition of Neuropsychotherapy.

However, some authors appoint some limitations to this approach to psychotherapy. Richter (2012) affirms that a neurobiological view of the human being may cause the psychotherapist to view the person as a "psychophysiological state", rather than a person that is a part of various complex social systems and fulfills different social roles, while interacting with other people that also are part of various social systems. Richter further adds that the decision-making process and the orientation of psychotherapy depend on reasons of interpersonal motives that the patient may have, and a neurobiological view might override this approach, in favor of a more "machinist" one, based on the patient's neurological functioning. Aligning with Richter's view, Fuchs (2004) states that the neurosciences may prove futile in explaining from a neurobiological perspective the interpersonal processes that occur during psychotherapy. Gauggel (2006) presents several arguments in favor of the neuropsychotherapy; stating that human behavior and experience have a role in shaping a person's self that goes beyond the biological, including also the social and the cultural aspects.

### 3. Objectives

This study aims to characterize and provide a summary of the existing literature about neuropsychotherapy across mainstream databases (EBSCO, B-on, Medline/PubMed, PsycINFO, Web of Science and Scielo), as well as clarify possible courses for future research. The characterization will include an analysis of the chronological and geographical (according to the authors' institutions) distribution of publications. The studies will also be described and characterized concerning its content via a studies' summary table. To the extent of our knowledge, there is no other literature review with a systematic approach to the search process that includes quantification and the temporal evolution of research about this particular topic.

### 4. Methods

The National Research Council (1999) emphasized the importance of the utilization of scientific databases and the peer-review process in the creation of rigorous scientific knowledge. Therefore, in order to retrieve all available scientific articles on the topic of Neuropsychotherapy, a research was conducted through six databases (EBSCO, B-On, Medline/Pubmed, PsycINFO, Web of Science and Scielo). The following research criteria were defined for article selection:

- The publication must be a scientific article. Other formats (e.g. conference posters) will not be included;
- The article must be available in one of the above-mentioned databases;
- The article must include the word "neuropsychotherapy" in the abstract and/or in the title, and the article main focus must either be neuropsychotherapy or an intervention that includes neuropsychotherapy, and it must specifically refer to that;
- The article must be published in a peer-reviewed scientific journal.

The following research terms were used in all databases: "Neuropsychotherapy", "Neuropsychotherapeutic", "Neuropsicoterapia", and "Neuropsicoterapêutico".

Using EBSCO, the following sub-databases were selected: Academic Search Complete, Psychology and Behavioral Sciences collection, Cochrane Database of Systematic Reviews, and MEDLINE Complete. The search was further refined by selecting the option "Search all my search terms", deselect expanders, and limit results to peer-reviewed journals. This search resulted in thirteen (13) entries.

Using B-On, the search was developed by selecting "Advanced Search", unchecking "Also search within the full text of the articles" and "Apply equivalent subjects", and checking the option "Peer Reviewed". The search resulted in 55 database entries.

In Medline/Pubmed, besides using the research terms mentioned above, we selected the option "search in title/abstract". The search wielded eight (8) search results.

While using PsycInfo, the search was conducted after unselecting "Include related terms" and selecting the option "peer-reviewed journals". The search wielded thirty (30) database entries. In Web of Science and Scielo, we did not select any advanced search options. Web of Science wielded thirty-two (32) search entries and Scielo wielded zero (0).

The search wielded in total a hundred and thirty-eight (138) results.

Due to duplicate removal, eighty-seven (87) entries were removed and fifty-one (51) entries remained. After title and abstract screening, twenty-eight (28) database entries remained. Twenty-three (23) search results were excluded; of which eighteen (18) were not a scientific article and five (5) did not refer neuropsychotherapy at all.

Of the twenty-eight (28) remaining entries, three (3) were excluded because the article fulltext was not available (the search entries referred an article, but after a thorough search and contacting the authors, no response was obtained and still no article was found), eight (8) articles did not directly discuss neuropsychotherapy and therefore were not relevant for this review (i.e. were not focused on the topic), and nine (9) were excluded due to language barriers (one Czech and eight German articles, with no translation available).

After the selection process, eight (8) articles were selected to be included for analysis in this review. This process is summarized in the flowchart (figure 1).

The articles were subjected to descriptive analysis, to characterize the chronological (through the publication dates, see figure 2) and geographical (through the authors' institutions, see

table 1) distribution of the publications. The articles also were analyzed and classified by their content (see table 2).



Figure 1 - Selection process flowchart

## 5. Results

After a thorough search through the main databases, eight studies were included in this review. The chronologic analysis (see Figure 2) indicates that the number of articles has been increasing since the first article published (Jønsson, Korfitzen, Heltberg, Ravnborg & Byskov-Ottosen, 1993), with most of the articles being published after 2005 (6 articles).



Figure 2 - Chronological Distribution of Publications

The geographical analysis (see table 1) shows that most articles (4 articles) are published by authors (15 authors) associated with German institutions (4 institutions). There are also articles published by Swiss (6 authors, 2 institutions and 1 article), Danish (5 authors, 1 institution and 1 article), Spanish (4 authors, 1 institution and 1 article), French (2 authors, 2 institutions and 1 article), and English (1 author, 1 institutions, and 1 article) institutions.

Table 2 shows a summary of the various studies included in this review. Of the eight studies, three can be considered primary literature and five secondary By primary literature, we refer to articles that present original research (i.e. randomized controlled trials) (Galvan & Galvan, 2017). Secondary literature refers to the scientific communications that review original research (i.e. literature reviews) (Carter, Griffin & Carter, 2006).

All three primary literature studies included in this review are clinical studies that focus on the effectiveness of therapeutic strategies that may be considered neuropsychotherapeutic. Of the three primary literature articles, two (Bachmann et al., 2018; Jønsson et. al, 1993) are randomized controlled trials (RCT) and one (Hofer et al., 2012) is a single-group clinical study. Bachmann et al. (2018) conducted a randomized clinical trial to test and compare the effectiveness of a mindfulness-based intervention against a psychoeducation-based intervention in ADHD, defining neuropsychotherapy by Grawe's (2007) definition. Jønsson et al. (1993) also conducted a randomized clinical trial to compare the effectiveness of an intervention program that consisted of aimed cognitive stimulation and neuropsychotherapy versus non-specific cognitive intervention. In this case, the authors' definition of neuropsychotherapy matches Ellis's (1989) and Judd's (1999). Hoffer et al. (2012) aimed to test the effectiveness of a neuropsychotherapeutic intervention program for post-stroke fatigue in

single-group design study, also matching the Judd's (1999) definition of neuropsychotherapy. All the studies' results, conclusions, and limitations are stated in table 2.

The secondary literature articles consist of five literature reviews, all of which discuss neuropsychotherapy. Bachmann, Lam, and Phillipsen (2016) discussed the neural effects of mindfulness practice and possible ways the said effects could be harnessed in therapy. The authors also reviewed eight studies, five of which focus on neuroimaging in mindfulness practitioners and three on clinical trials of mindfulness-based intervention programs. Fuchs (2004) disserted about neurobiological research relevant for psychotherapy and alerted to some conceptual problems that may arise from this new approach. García-Molina et al. (2014) disserted about the utility of neuropsychotherapy as a brain rehabilitation tool and discussed several theoretical aspects of psychotherapy with brain-injured patients. Walter, Berger, and Schnell (2009) reviewed several studies related to the concept of neuropsychotherapy and proposed a novel working definition of neuropsychotherapy (as discussed above). Ward, Delrue, and Plagnol (2017) also reviewed several articles related to neuropsychotherapeutic theoretical models, and proposed a new one, using trauma as an example and referring several illustrative cases.

Country	Authors	Institutions	Articles	
Germany		15	4	4
Switzerland		6	2	1
Spain		4	1	1
Denmark		5	1	1
England		1	1	1
France		2	2	1
Total		33	11	9*

### Table 1 - Worldwide geographical distribution of publications

\*The total number of articles (9) exceeds the actual number (8) because one of the articles is the result of a collaboration between English and French institutions.

Table	2 - Studies'	summary	

Article	Source type	Article description	Sample (if applicable)	Results/Conclusions	Notes
Bachmann et al., 2018	Primary literature	Randomized and controlled trial to compare intervention strategies in Attention- Deficit/Hyperactivity Disorder (ADHD) in adults, namely a mindfulness- based intervention program (Mindfulness Awareness Practice, or MAP), and psychoeducation (PE), with an assessment of therapy effectiveness with a working memory task (n- back task) during fMRI. ADHD symptoms were also assessed via the Conners Adult ADHD Rating Scales (CAARS).	<ul> <li>Sample: n=42;</li> <li>21 participants per group;</li> <li>1 control group (PE);</li> <li>1 experimental group (MAP);</li> <li>Sample age: 19 to 61 years;</li> <li>Participants inclusion criteria: <ul> <li>Diagnosis of ADHD combined</li> <li>subtype or inattentive subtype</li> <li>(DSM-IV criteria);</li> <li>Participants were not doing</li> <li>pharmacological therapy for ADHD</li> <li>(stimulants or atomoxetine) 3</li> <li>months before and during study</li> <li>participant I.Q. &gt; 85;</li> <li>Participants were also excluded</li> <li>if they matched the criteria for</li> <li>schizophrenia, bipolar disorder</li> <li>type I, or had any of the following</li> <li>characteristics: substance abuse</li> <li>dependence, autism, acute</li> <li>suicidality, self-injurious behavior</li> <li>or neurological disorders;</li> <li>Participants must not have any</li> </ul> </li> </ul>	<ul> <li>Both groups have shown improvement in n-task performance. However, no significant main effect of therapy and no significant interaction effect were found.</li> <li>Both the CAARS Blind Observer Rating and the CAARS self-rating indicated that there was a significantly lower level of ADHD symptoms in both groups. Again, no effect of therapy nor interaction effect was found in between-subjects comparison.</li> <li>The experimental group manifested higher activation in several areas when comparing post- with pre- intervention. These areas were mainly located in the bilateral inferior parietal lobule, right posterior insula, and right precuneus. Like in the previous measures, no effect of therapy was found.</li> </ul>	<ul> <li>Study limitations mentioned by the authors:</li> <li>The study results were based only in an exploratory analysis, so there is no clear cause for the improvement after therapy;</li> <li>The duration of the intervention program (8 weeks) may not be enough to exert a significant neurobiological effect;</li> <li>The fMRI results should be carefully interpreted, since mindfulness practice may activate different brain areas depending on the practitioner's experience.</li> </ul>

Article	Source type	Article description	Sample (if applicable)	Results/Conclusions	Notes
Hofer et al., 2012	Primary Literature	Single group clinical study of a neuropsychotherapeutic intervention program for post-stroke fatigue with pre- and post-intervention assessment with a self- assessment questionnaire for mental fatigue (SQfMF).	<ul> <li>Sample: n=8;</li> <li>Sample by gender: 5 males, 3 females;</li> <li>Sample age: 20-61 years (Mean: 48);</li> <li>Stroke subtypes: 2 hemorrhagic and 6 ischemic strokes.</li> <li>Time since stroke: 4 to 65 months (Mean: 18 months).</li> </ul>	<ul> <li>A significant difference emerged from the end-therapy to the pre- therapy assessment with a marked decrease of fatigue;</li> <li>The study participants claim to h attained the goals formulated at th beginning of the intervention.</li> </ul>	The authors mention the following limitations: - Small sample size and lack of a control group; have - The fact that this intervention program is included in a larger neuropsychotherapeutic program, therefore not being possible to distinguish the effects of this specific intervention from the effects of the larger program; - The use of self-report measures both during the intervention and in the pre- and post-intervention assessment.
Jønsson, Korfitzen, Heltber, Ravnborg & Byskov-Ottosen, 1993	Primary Literature	Randomized controlled clinical trial of an intervention program involving aimed cognitive stimulation and neuropsychotherapy vs. non- specific cognitive stimulation in patients with multiple sclerosis (MS).	<ul> <li>Sample: n=40;</li> <li>Sample by gender: 19 females and 21 males;</li> <li>Mean age: 44,5 years (SD=8,3);</li> <li>Experimental group (intervention program) n=20;</li> <li>Control group (non-specific cognitive stimulation) n=20;</li> <li>Inclusion criteria: Participants must match the criteria for an EM diagnosis;</li> <li>Exclusion criteria: Participants must not match the criteria for any disorder besides EM.</li> </ul>	Results: - The experimental group registered improvements in visual perception and visuospatial memory, as well as in depressive symptoms. This group has also reported lesser anxiety, although the results were not statistically significant. - The control group registered improvements in visuomotor speed.	The authors acknowledged the following limitation: - The cognitive assessment battery used may have not been ideal for assessing the full extent of the treatment effects.

Table 2 - Studies' summary (continuation)

Table 2 - St	udies' summary	y (conti	nuation)	
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Article	Source type	Article description	Sample (if applicable)	Results/Conclusions	Notes
Bachmann, Lam & Phillipsen, 2016	Secondary literature	Narrative review of the effects of mindfulness practice in neural activation and the effectiveness of mindfulness-based intervention programs for ADHD adult patients.	<ul> <li>8 studies reviewed</li> <li>5 neuroimaging studies in mindfulness practitioners;</li> <li>3 clinical studies of ADHD mindfulness-based intervention.</li> </ul>	Neuroimaging studies results shown increased activation in prefrontal and parietal areas in novice practitioners, and reduced activation of some prefrontal and parietal areas, as well as in the default- mode network (DMN), and increased activation of striatum, insula, and anterior cingulate cortex in advanced practitioners. Clinical studies shown reduced ADHD symptom manifestation, especially in hyperactivity, impulsivity, and attention control.	The authors mention some limitations in the reviewed studies, mainly about the sample sizes, in the study control conditions, and the randomization techniques. Furthermore, the authors also address the need to study eventual correlations between neural activation and clinical improvement in this type of intervention program.
Fuchs, 2004	Secondary Literature	Literature review about neurobiological research relevant for psychotherapy and discussion of some conceptual problems associated with this new approach.	Non-applicable	The author summarizes the review by affirming that there are all kinds of positions in the antagonism-endorsement about this particular paradigm. The author goes on by saying that the research at the time of the writing was still preliminary. The author also acknowledges the possibility of using neurobiological models to improve the design of psychotherapeutic interventions. The author finishes by warning that it may be futile to expect that the interpersonal processes that occur during psychotherapy will ever be completely explained by neuroanatomical knowledge.	

### Table 2 - Studies' summary (continuation)

Article	Source type	Article description	Sample (if applicable)	Results/Conclusions	Notes
García-Molina, Roig-Rovira, Enseñat- Cantallops & Sánchez- Carrión, 2014	Secondary Literature	Literature review about neuropsychotherapy as a tool in brain damage rehabilitation, through the description of the theoretical aspects of psychotherapy with neurological patients	Non-applicable	The authors conclude that the acknowledgment of the need for neuropsychotherapy as a neurorehabilitation strategy between neurological healthcare professionals has grown over the last years. The authors also advance that the aim of neuropsychological rehabilitation goes beyond recovery and maintenance of the patients' cognitive functions, with its true aim being the improvement of quality of life, with neuropsychotherapy being a fundamental tool for such goal.	
Walter, Berger & Schnell, 2009	Secondary literature	Narrative review about the concept of neuropsychotherapy, with a proposal of a working definition for the said concept, a review of neuroimaging studies of psychotherapy and a discussion about the ethical issues of this possible field of research and clinical practice.	Non-applicable	The authors conclude that neuroscience is being integrated with psychotherapy, and suggest a working definition for neuropsychotherapy consisting of the identification of neural mediators and functional targets, determination of therapeutic routes to the said targets, and designing the referred therapeutic routes. The authors also point out that the discussion about neuropsychotherapy should not only include its possible merits but also its limitations.	

### Table 2 - Studies' summary (continuation)

Article	Source type	Article description	Sample (if applicable)	Results/Conclusions	Notes
Ward, Delrue & Plagnol, 2017	Secondary literature	Literature review to describe the neuropsychotherapeutic perspective applied to practical psychotherapy using the example of trauma, with a presentation of illustrative clinical cases.	<ul> <li>Sample: n=4</li> <li>The described cases match the criteria for PTSD;</li> <li>Female 91 years old patient;</li> <li>Female 92 years old patient;</li> <li>Female 93 years old patient;</li> <li>Male 91 years old patient.</li> </ul>	The authors conclude by summing up the various theoretical strands that compose the theoretical frame of neuropsychotherapy, and through the example of trauma, they explain how the integration of neuroscientific knowledge might answer some questions about the etiopathogeny of disorders.	

## 6. Discussion

In the present work, we reviewed all the studies related to neuropsychotherapy available in the mainstream databases (namely EBSCO, B-on, Medline/Pubmed, PsycINFO, Web of Science and Scielo). After the search and screening process, eight articles were eligible to be included in the review.

Through the chronological distribution of publications on the topic of neuropsychotherapy, one can observe that the number of publications has been on the rise for the last few years, which suggests an increase in the interest in this topic. This is consistent with Goss's (2016) findings, and with the seemingly rising trend of the neuroscience of psychology studies.

The geographical distribution shows that the majority of the research is being conducted in Germany. This may be because Grawe's (2007) work, *Neuropsychotherapy - How neurosciences inform effective psychotherapy*, was first published in German, and therefore it may have captured the attention of the German researchers due to geographical proximity and linguistic compatibility.

Of the eight included articles, three were primary literature sources, namely two RCT (Bachmann et al., 2018; Jønsson et al., 1993) and one clinical study with single-group design (Hofer et al., 2012), and five were secondary literature sources (mainly literature reviews). The summary of the included studies can be consulted in table 2.

The primary literature studies included represent the only intervention procedures described as neuropsychotherapy in scientific databases. However, it should be considered that there are many other interventions described that may fit the criteria for being considered neuropsychotherapeutic in nature, but are not described as such (e.g. neuromodulationassisted therapy). It is important to clarify that the articles referring to those interventions were not included in this review since its purpose was to characterize the available scientific literature that clearly identified neuropsychotherapy (i.e. described by the authors as neuropsychotherapy).

In this study, there are several limitations to be taken into account. Due to language barriers, several articles were excluded from this review (eight articles in German and one in Czech). These articles, if eligible, should be considered in a future review.

Several limitations were also found in the included primary literature studies, namely:

- Small sample sizes (Bachman et. al, 2018; Hofer et. al, 2012);
- Lack of a control group (Hofer et. al, 2012);
- Neuropsychotherapeutic interventions were included in larger intervention programs, therefore making it unclear the true contributions of neuropsychotherapy (Hofer et. al, 2012; Jønsson et. al, 1993);
- The use of self-report measures may result in the report of perception of improvement, and not actual improvement (Hofer et. al, 2012);

- The use of assessment instruments that may not have been ideal for evaluation of the intervention impact (Jønsson et. al, 1993).

In the secondary literature studies, the main limitation is the fact that none of the articles mentions the inclusion criteria used for article selection.

In order to establish consensus and generate high-quality evidence for this field, several measures could be undertaken. First and foremost, the creation of specialist discussion groups would be advised, in an attempt to generate an agreement and unify the different approaches and models of neuropsychotherapy. An effort should be made to clarify the possible interconnection between Ellis's (1989) and Judd's (1999) perspective (neuropsychotherapy as a tool for neurological rehabilitation) and Grawe's (2007) perspective (neuropsychotherapy as a neurologically informed psychotherapy). Although both perspectives draw from the same principles to achieve the same goals, to the extent of our knowledge no author has ever unified both perspectives. Namely, both perspectives aim to use neuroscientific knowledge to improve the quality of psychological intervention, with the aim of improving the patients' quality of life and general functioning. However, as referred, no author acknowledges these similarities between approaches. In addition, experts should strive to produce unified formal criteria for what qualifies as a neuropsychotherapeutic intervention. Other possible measures would be the elaboration of more clinical studies; particularly more randomized controlled trial with better control conditions and study design (such as a clearly defined neuropsychotherapeutic intervention in the experimental groups, and control groups with placebo and waiting list condition), and compared efficacy and effectiveness trials featuring possible neuropsychotherapeutic interventions and standard interventions. In this sense, Grawe (2007, p. 437) proposed guidelines for a neuropsychotherapeutic intervention following his theoretic model. However, there is no study describing its effectiveness, and so this can be a possible investigation route. We are aware of a scientific journal that seeks to fill some of the gaps previously referred (i.e. The International Journal of Neuropsychotherapy - IJNP, 2019). However, since it is not indexed in any of the consulted databases, its articles did not fulfill the inclusion criteria for this review and therefore were not included.

In conclusion, with this review, we clarify and summarize the existent scientific literature about Neuropsychotherapy. Additionally, we suggest possible courses for future research for the advancement of the field.

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## 8. Annex - Theoretic Supplement

### Psychotherapy and Clinical Psychology: A theoretical frame

Psychotherapy, since its birth, has divided scholars between the different theoretical approaches of the larger domain of clinical psychology (Gleitman, Gross & Reisberg, 2011). American Psychological Association (APA) (2019) distinguishes five different approaches to psychotherapy: psychanalysis and psychodynamic, behavior, cognitive, humanistic, and integrative psychotherapies.

In order to fully understand psychotherapy, its evolution and why it has so many different theoretical approaches, each with its strategies and techniques, it is necessary to establish a parallelism between psychopathology, psychology, sociology, as well as with the cultural context and scientific thinking across times (Norcross, VandenBos & Freedheim, 2011).

While there are written records of mental health studies since the VII century (found in old Islamic texts, see Haque, 2004), the first steps of psychotherapy as we know it today can be retraced to the final of the XVIII century, in two distinct events:

- The development of moral treatment, by Phillipe Pinel (Pereira, 2004);
- The creation of mesmerism, by Franz Anton Mesmer (Goodwin, 2015).

Moral treatment is born from the rising of the inductive scientific method that characterizes the Renaissance movement of the XVII and XVIII centuries (Carlson & Dain, 1960). According to Pereira (2004), Phillipe Pinel, a French psychiatrist, noticed that the conventional psychiatric treatments of his time (namely bloodletting and physical punishments) were ineffective, and so sought a more effective treatment strategy. This strategy focused on the individualized and compassionate care, and on the effects of the environment on psychiatric health (both aspects are fundamental characteristics of modern psychotherapy). In practice, moral treatment consisted in involving patients in occupational therapy, religious exercises, entertainment activities, and in individual conversations with hospital staff (Pereira, 2004). Norcross, VandenBos and Freedheim (2011) state that an individual plan was formulated for each patient, keeping in mind their personal interests.

Mesmerism draws his name from Franz Anton Mesmer (1734-1815), a german doctor that developed a procedure for treating hysteria based on the animal magnetism theory, which he also developed (Norcross, VandenBos & Freedheim, 2011). This theory was later considered non-scientific. However, mesmerism continued to gather followers, eventually attracting interest from the scientific community. Mesmerism was later renamed as "Hypnosis", and was again used as a technique to treat hysteria by Jean-Martin Charcot (1825-1893), a French neurologist, considered the father of modern neurology (Teive, Chien, Munhoz & Barbosa, 2008).

Charcot's work about hysteria eventually attracted Sigmund Freud's attention. (Goodwin, 2015). Sigmund Freud (1856-1939), an Austrian neurologist interested in disorders of the nervous system (particularly in hysteria), sought out the contact of several specialists in that

field; the most known of which Charcot and Josef Breuer. With Charcot, Freud learned about hypnosis, which later contributed to his theory of unconscious. Josef Breuer (1842-1925), an Austrian physician, presented the Anna O. case to Freud, which led to Breuer and Freud's publication of "Studies on Hysteria", considered the founding event of psychanalysis and the catharsis method (Kenny, 2016). While developing his theory of psychanalysis, Freud also attempted to explain mental processes with neuro-physiological knowledge (Freud, 1895, cit. in Grawe, 2007), however, he soon dropped that project (Goodwin, 2005). Freudian psychanalysis is centered on the concepts of unconscious mind, defense mechanisms, structural theory, and many more (Kenny, 2016).

Lothane (2006, cit. in Kenny, 2016) states that psychanalysis is simultaneously a psychotherapeutic framework, a theory of personality, and an investigation tool. Initially, Freudian psychanalysis emphasized catharsis and repressed sexual instincts, which contributed to the separation of several followers of this approach. This caused a ramification in the psychodynamic approach (Goodwin, 2015). Carl Jung (1875-1961), a Swiss psychiatrist and Freud's student, after falling apart with his mentor, developed analytical psychology - a psychodynamic approach to personality that focuses on individual psyche and on concepts like archetypes, symbols, personal and collective unconscious (Kenny, 2016). Alfred Adler (1870-1937), an Austrian medical doctor, was part of an informal discussion group formed by Freud, until he and several followers dissented from traditional psychoanalysis. Adler went on to develop his own theory of the human psyche, individual psychology (Kenny, 2016). Individual psychology is based on the individual evaluation of the world, and its consequences on the individual. It takes into account concepts like compensation, resignation, over-compensation and inferiority complex (Goodwin, 2015). All of these approaches to psychology developed several ramifications, and were highly influential across most of the theoretic approaches to psychology. Psychodynamic and psychanalytical psychotherapy have suffered several changes across time, and are still practiced today.

During the first half of the XX century, psychodynamic theories were the predominant approaches to clinical psychology and psychotherapy (Goodwin, 2015). Despite this, influenced by Darwinian Theory, human behavior researchers and theorists have felt the need to adopt a more quantifiable perspective in their studies, employing methods similar to the ones used in natural sciences and starting to take an interest in animal behavior and learning (Parot, 2001). In fact, we can trace the first steps of the behaviorist approach to Alexander Bain (1813-1903), a Scottish philosopher who asked the following question: "When someone performs an action for the first time, does he or she do it in response to an exterior solicitation, or because he or she wants it?" (Bain, 1855, cit. in Parot, 2001); having Bain answered his own question by stating that it is by accident, and should the accident have beneficial consequences for the individual, he or she will repeat it and it will turn from a spontaneous act to a voluntary one (Bain, 1855, cit. in Parot, 2001).

Influenced by Bain, Darwin, and other researchers, Edward L. Thorndike (1874-1949), an American psychologist, studied the laws of learning by designing several experiences

popularized as the "Thorndike puzzle boxes", in which an hungry cat was placed inside the box, and would be rewarded if he managed to escape the box (Parot, 2001). Through those experiences, Thorndike inferred that animals associated the behavior with the response (in this case, the reward), and called this association the "law of effect" (Thorndike, 1898; cit. in Parot, 2001).

While Thorndike studied the behavioral law of effect, Ivan Pavlov (1849-1936), a Russian physiologist, developed a research project about the triggering of gastric secretion in dogs. By conditioning a previously neutral stimulus, Pavlov was able to elicit gastric secretion in dogs without using food stimuli. Thus, Pavlov had just discovered what we now call of classic conditioning.

These two researchers set the foundation for behaviorism. However, behaviorism as a major theoretical approach to psychology was only founded later, by John Watson (1878-1958) and his manifesto, "*Behaviorist Manifesto*" (Watson, 1913, cit. in Goodwin, 2015). In the manifesto, Watson affirmed that introspective psychology of subjective nature should give way to an objective behavioral psychology that emphasized the relationship between stimuli and response (Harzem, 2004). Watson's main works were "*Behaviorism*", in which he exposed most of his behaviorist theory (Goodwin, 2015), and "*Psychological Care of Infant and Child*", in which he discussed children educative methods that followed the principles of his behaviorist theory (Parrot, 2001).

After Watson's behaviorism, a new theoretical strand within behaviorism began to gain strength: Neobehaviorism (Amsel, 1989). According to Amsel (1989), neobehaviorism is characterized by including the concept of "organism" in the usual "stimuli-response" relationship, in the sense that the cognitive functioning (under the form of intervening variables) of the organism influences the response to stimuli. The main representatives of this theoretical strand are Edwin Guthrie (1886-1959), Edward Tolman (1886-1959), and Clark Hull (1884-1952) (Goodwin, 2015). Guthrie's main contribution was the concept of contiguity (the experiencing of things together), Tolman introduced purposive behavior theory (Leary, 2004; Goodwin, 2015) and Hull attempted to define behaviorist psychology as a hypothetical-deductive system (Parot, 2001; Leary, 2004; Goodwin, 2015).

Later, radical behaviorism would resurface with one researcher that would become one of the leading experts and main authors in the field of behaviorist psychology: Buhrrus Skinner (1904-1990). Skinner's main contribution was the development of the concept of operant conditioning, and the role of reward in behavior learning and frequency (thus following Bain, and later Thorndike) (Goodwin, 2015).

While behaviorism by itself is not enough to sustain a psychotherapeutic intervention, it greatly influenced therapeutic practice with several therapeutic strategies and techniques, the so-called "behavior therapies" (Goodwin, 2015). In fact, Parot (2001) states that behaviorism influence is felt mainly in mental health and education.

While behaviorism was developing in the United States of America, European psychologists focused on what would now be considered the roots of cognitive psychology. Goodwin (2015)

enumerates two main contributors to the birth of this movement: Jean Piaget (1896-1980) and Frederick Bartlett (1886-1969). Jean Piaget is celebrated for his work in developmental psychology and the introduction of the concept of schemata, widely used in cognitivebehavioral therapy (Schultz & Schultz, 2011). Bartlett is noted for his work on memory, *"Remembering: A Study in Experimental and Social Psychology"* (Bartlett, 1932; cit. in Goodwin, 2015), which described the active role of the individual on the organization of mnesic content.

Although the birth of cognitive psychology cannot be credited to individual researchers, Schultz and Schultz (2011) affirm that two scholars contributed with work that is today considered breakthroughs of cognitive psychology: George Miller (1920-2012) and Ulric Neisser (1928-2012). Miller is remembered by its research on short-term memory capacity and the founding of the Center for Cognitive Studies (Schultz and Schultz, 2011). Neisser published several reference works, namely *Cognitive Psychology* (1967, cit. in Schultz and Schultz, 2011) and *Cognition and Reality* (1976, cit. in Schultz and Schultz, 2011). Neisser is particularly important to psychotherapy, having defended a practical application of cognitive psychology and claiming that cognitive psychology should be able to apply their findings to practical problems, and help people to deal with everyday issues in their lives (Schultz and Schultz, 2011).

Cognitive psychology is considered to be "psychology regaining consciousness" (Schultz and Schultz, 2011, p. 353). Renegading radical behaviorism, cognitive psychology's emphasis resides on the process of knowing, rather than just responding to stimuli. If one wants, a parallelism with Neobehaviorism and its concept of "intervening variables" can be established; the main difference being that in cognitive psychology the intervening variables are the protagonists, and not merely components of behavior (Goodwin, 2015).

Behaviorism and cognitivism gave birth to another prominent psychotherapeutic approach: cognitive-behavioral therapy. Cognitive-behavioral therapy is defined as "a class of interventions that share the basic premise that mental disorders and psychological distress are maintained by cognitive factors" (Hofmann, Asnaani, Vonk, Sawyer & Fang, 2012). Hoffman and colleagues state that Aaron Beck (1921-) and Albert Ellis (1913-2007) pioneered this approach. The cognitive movement was not the only theoretic current "rebelling" against behaviorism. Humanistic psychology appeared in the middle of the XX century, as a counter-current against the "mechanichal, impersonal, hierarchical, elitist psychoanalytical establishment and overly scientistic, cold, removed behaviorism" (Cushman, 1992; cit. in Goodwin, 2015). The core principles of the humanistic perspective, as stated by Buhler (1971) are the study and understanding of the individual as a whole, the need to understand the life narrative of the individual, the role of motivation in human life, and the "importance of the end goal for the healthy person" (Buhler, 1971). Goodwin (2015) states that there were two main psychologists in the humanistic movement of psychology: Abraham Maslow (1908-1970) and Carl Rogers (1902-1987). Maslow's main contribution was the study of motivation, with the widely known model of the hierarchy of needs and the ultimate goal of self-actualization (Maslow, 1943). Rogers developed the client-centered therapy, an approach to therapy that follows the tenets of humanistic psychology (Rogers, 1946). Rogers (1946) believed that in order to produce beneficial results in therapy, the therapist should create a therapeutic environment that would enable the client to take control of his or her life and strive for self-actualization. This environment should abide to three conditions (Goodwin, 2015): (i) the therapist must be honest with the client, so that the therapist may serve as a model of emotional health intended in the client; (ii) the therapist must have a posture of full acceptance, in the sense that he value the client simply by the virtue of being human; and (iii) the therapeutic relationship must be based on empathy.

The last psychotherapeutic approach enumerated by APA (2019) is integrative psychotherapy. Therapists that follow this approach "blend in elements from different approaches and tailor their treatment according to each client's needs" (APA, 2019). According to Zarbo, Tasca, Cattafi and Compare (2016), most of the psychologists use more than a single theoretical orientation in their practive, with the median number of approaches used being four. Neuropsychotherapy then can be considered an integrative approach to psychotherapy, since it strives towards using neuroscience to orient and gauge the effectiveness of techniques from different psychotherapeutic approaches (Grawe, 2007).

### Brain, Behavior and Neuropsychotherapy

In the course of history, the origin of human behavior has always been one of the main points of interest of humankind. Kolb and Whishaw (2014) appoint three main chains of thought: mentalism, dualism and materialism.

Mentalism is the most ancient of the referred chains of thought, remounting to ancient Greece. Aristotle, alluding to the mythological history of Cupid and Psyche, affirms that the origin of intellectual activity is in the human psyche, with it being responsible for life and death (Matthews, 2008). In Aristotle theory, the human brain didn't had any relationship with behavior. The psyche was an immaterial entity, independent of any physical restrictions. This theory is a good illustration of the philosophical position of Mentalism: the mind (or psyche) exists independently of the body, being the first responsible for the behavior and the second being only a vehicle (Carlson, 2002).

Dualism is a relatively recent philosophical current, when compared to Mentalism. Proposed by Descartes (1663), Mentalism defends that the human brain is a point of connection between body and mind, although the latter remains a separate entity. In this case, the body would be responsible for the most basic activities, like breathing, eating or sleeping, and the mind, still a immaterial entity, would be entrusted with rational behavior. The mind receives and transmits information to the body through the pineal gland, being this organ a communication point between the two entities. Descartes' theory, though characterized by the dualism "immaterial mind-physical body", recognizes the body (and the brain) as responsible for some behaviors, in spite of relegating to the immaterial and incorporeal mind the so-called "higher functions" (Damásio, 2011), being this the main point of distinction between mentalism and dualism.

Materialism refers to the idea that, in a general way, everything can be explained through material and physical factors (Armstrong, 1978). Applied to the study of behavior, materialism stands by the notion that the nervous system completely explains rational behavior, without the interference of an incorporeal mind (Rekret, 2018).

According to Kolb and Whishaw (2014), this theory became especially popular after the evolutionary theories of Charles Darwin and Alfred Russel Wallace. The referred theories, when associated with Mendel's genetic inheritance theory, as well with the general concepts of epigenetics bring us three assumptions that are fundamental to the study of the brain-behavior relationship (Kolb and Whishaw, 2014):

<u>-If all the animal species are related and have a common ancestry, so must their brains:</u> Nowadays, it is well known that the brain cells of all the animals are quite similar, so they must share some degree of kinship in an evolutionary perspective. In addition, the encephalon of the different species is very similar, regarding both morphology and cytoarchitecture; so much, so that certain studies of the nervous system of various animals may be generalized to some extent the human being.

- <u>If all animal species are related and have a common ancestry, so must their behavior:</u> This assumption is evident in certain behavioral expressions innately present in every human being. Emotional facial expressions are a good example of this: every human being shares similar facial expressions when reacting to some emotions, even when they originate from different cultural contexts.

- <u>Although both the brain and the behavior of complex animals (including humans) evolved</u> <u>from the brain and behavior of simpler animals, both continue to depend on learning:</u> Of course, not all behavioral expression is innate. Most behavioral expressions are learned throughout life, and this learning will shape not only the individual in behavioral and neurological aspects, but also the species in terms of genetic aspects.

Following this line of reasoning, in order to be able to understand the relation brain-behavior of the current human being, it is necessary to be aware of the evolutionary process of the human encephalon.

In a chronological scale, two million years separate the first individuals of the genre *Homo* (*Homo habilis*) and *Homo sapiens sapiens*. Beyond the chronological scale, they are also separated by an increase in cortical volume of about 700 cm<sup>3</sup> (Holloway, Broadfield & Yuan, 2004). In addition to cortical volume, other significant differences mark the evolution of the human brain, specifically in terms of proportional volume. The increase in cortical volume was not homogenous. Bailey and Geary (2009) state that the frontal lobe was the cortical area that had a greater increase in volume. This is consistent with the sociological progression of human beings. The frontal lobe is associated with several different functions, such as cognitive flexibility, decision-making and the understanding of social rules (Kolb and Whishaw, 2014). Therefore, a correlation can be made between the increase in volume of the frontal cortical area, the proliferation of human race and the complexification of human society.

In order to understand the relationship between brain and behavior, it is also necessary to have at least elementary knowledge of the functioning of neural anatomy. Kandel and colleagues (2013) affirm that it is possible to have a greater understanding of how the nervous system produces behavior by taking into account 5 features:

- The structural components of individual nerve cells;
- The mechanisms of communication between nerve cells;
- The patterns of communication between central nervous system (CNS), peripheral nervous system (PNS) and muscles and glands;
- The relationship between the different patterns of communication and different behavior;
- How nerve cells and their communication are modified by experience.

There are two main different types of cells in the nervous system: neurons and glia (Kandel, 2013).

The neuron typically has four components: the soma or cell body, dendrites, axon and presynaptic terminal. The cell body is the center of the cell, it contains the nucleus, and usually is connected to the dendrites and the axon (Kandel, 2013). The communication between neurons is made via an electrochemical process known as synapsis. The electrical part of the synapsis occurs when the entrance of positively charged ions enter the neuron, causing a depolarization of the cell and triggering an action potential. The electric signal is carried along the axon until it reaches the presynaptic terminals. Upon receiving the signal, presynaptic terminals release unto the synaptic cleft (the space between the communicating neurons) chemical substances known as neurotransmitters. These neurotransmitters will then influence the triggering or inhibiting of an action potential in the post-synaptic neuron (Kandel, 2013). Kandel (2013) signal a key principle of brain function: the information conveyed by action potentials does not depend on the form of the signal, but by the course it takes.

Glia are cells that support the neurons and its numbers are vastly superior - glia outnumber neurons by two to ten times in the CNS (Kandel, 2013). Glial cells' function is not entirely known yet. They form the myelin sheath that insulates the axon, and thus facilitates the propagation of the electrical signals. They are also envolved in the regulation of the chemical environment surrounding the neurons, in the supplying process of the neuron, and in denditric arborization protection via the destruction of pathogens and the removal of dead neurons (Kolb and Whishaw, 2014).

On a macroanatomical level, the nervous system can be generally divided in central nervous system, which includes the brain and spinal chord and the peripheral nervous system, which includes the somatic nervous system (responsible for transmitting sensory information and motor impulses) and the autonomic nervous system (mediates internal biological funcions). The brain can be further divided into several sections: the prosencephalon, the mesencephalon, and the rhombecephalon (Kandel et. al, 2013). The prosencephalon can be subdivided in telencephalon and diencephalon. The telecenphalon includes most of the structures responsible

for "higher mental function", like the cerebral cortex, the limbic system and basal ganglia. The diencephalon incudes structures related to emotional regulation, like the thalamus and the hypothalamus. The cerebral cortex can be divided into several sections, delimitated by sulci and gyri. Most theorists distinguish between four major functional areas: the temporal lobe, the frontal lobe, the parietal lobe and the occipital lobe. The temporal lobe is mostly associated with hearing, language and memory function; the frontal lobe is considered the brain executive and motor center; the parietal lobe is mainly associated with associating information from the different sensory inputs, proprioception and laterality; and the occipital lobe is associated with visual processing. Each area divides further within itself (Kolb and Whishaw, 2014).

Behavior arises from inhibition and activation of different neural circuits within and between the aforementioned areas. Although the exact process of the creation of the phenomenon of consciousness is not yet fully explained, it is generally agreed that it arises from the interconnectivity of all areas of the brain (LeDoux, 2002).

The brain-behavior and the brain-mental health relationships are well documented in the current scientific establishment. Maia (2017) refers Kandel's (1998) five principles as the basis of the understanding of mental disease from a genetic, neural and behavioral standpoint. The principles are:

- Principle 1- Every mental process derives from operations of the brain That which is commonly called mind depends on a series of neural processes. The brain regulates not only common motor functions (e.g. walking), but also all the complex cognitive and emotional actions (e.g. speaking, creating art, reading). Therefore, every behavioral disorder is a result of brain function, even when the said disorder is environmental in origin (Kandel, 1998);
- <u>Principle 2- Genes and their protein products determine the neural circuits and the</u> <u>details of their functioning</u> - According to this principle, genes (and combinations of genes) exert a significant control over behavior, by determining the predisposition of the individual to some behaviors. Therefore, one's genotype contributes to the development of mental illnesses (Kandel, 1998).
- Principle 3- Altered genes do not explain all of the variance of a major mental illness -The genotype is not enough to predict the development of mental illness. Citing Kandel (1998), "Just as combinations of genes contribute to behavior (...) so can behavior and social factors exert actions on the brain by feeding back upon it to modify the expression of genes and thus the function of nerve cells".
- <u>Principle 4- Alterations in gene expression induced by learning translate into patterns</u> <u>of neuronal connection</u> - Learning will alter gene expression, neural circuits, and neural functioning. These changes play a major role both in the biological foundation of individuality and in the rising and maintenance of mental disorders (Kandel, 1998).
- <u>Principle 5- Psychotherapy as an effective process</u> The long-term changes worked by psychotherapy are provoked by learning. Learning, in turn, produces changes in gene

expression that have an impact in neuronal connections and consequently in the anatomical structure of the brain.

With this, the importance of understanding brain activity for psychotherapy becomes clear, and thus answers one of the greatest methodological issues in clinical psychology and psychotherapy: biological markers of change due to psychotherapy (Kazdin, 2007; cit. in Ecker, 2018). This issue has also contributed to the perpetuation of the "mind-body" or "materialism-mentalism" discussion; even though there have been records of abnormal neural activity in psychiatric disorders for quite some time (see Goss, 2016).

In a systematic review, Goss (2016) shows that neuroscientific interest in the neural changes of psychotherapy has been rising, which translates to an exponential growth of the number of publications about the neurological functioning and the psychotherapy-produced changes in the mental illness patient.

Grawe (2007) states that although some theoretic concepts might be revised, the growing interconnection between psychotherapy and neurosciences does not mean that psychotherapeutic theoretic models will suddenly stop being used. As referred before, just as the success of psychotherapy causes an impact in neural functioning, the said impact will only occur if the psychotherapy is correctly executed. This means that it is not necessary to be an expert in neurosciences in order to achieve brain-level changes in an individual. Grawe exemplifies this by stating that several non-health professionals (e.g. teachers, coaches) also achieve brain-changes in other individuals without having any neuroscientific knowledge.

It is also important to emphasize that neuroscientific knowledge, by itself, is not enough in order to produce the beneficial effects that result from psychotherapy. A neuroscientist without training and education in clinical psychology and psychotherapy does not have the necessary tools to establish a clinical psychology practice (Ecker, Ticic & Hulley, 2012).

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