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Unpacking the interplay between valence and semantics in emotion processing: electrophysiological and neuroimaging correlates in healthy and clinical populations

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Abstract

Emotions are acquired through our personal experiences and similar to other semantic concepts, they are stored in the brain as language-based concepts. Processing an emotion involves the automatic estimate of its affective content – the evaluation in terms of positive or negative valence; its associated semantic content – the conveyed meaning; and its level of activation – named arousal. The aim of the thesis is to investigate the affective and semantic variables that shape the semantic space of emotions examining the electrophysiological and neuroimaging correlates in both healthy and clinical populations.

Studies 1 (n=30, published) and 2 (n=34, published) used an affective priming paradigm to study the interaction between the affective and semantic content during the automatic elaboration of emotional words. By using pain as a model, I hypothesized a faciliatory effect in processing the valence of a negative word when preceded by a pain word rather than a negative or positive word unrelated to pain. Study 1 showed a significant interaction between the valence and the semantics of the stimuli which generates a specific facilitatory response to pain. In Study 2, ERP analyses revealed no effect of pain during early-stage processing (N400), but a larger waveform was observed when the negative word was preceded by a pain word during late-stage processing (LPP). This suggested the cognitive system required longer time to generate a response to specific semantic content, highlighting the different time course of the affective and semantic content.

In Study 3 (n=34, *in preparation*) I used an emotional fluency task which instead relies on voluntary processing. Results revealed a tendency to recall more negative words than positive ones and, an additional interaction with the arousal where individuals produced more positive words with high arousal compared to low arousal positive and negative words. Additionally, the order in which individuals produced the words was predicted by the semantic relatedness among consecutive words, but not by the valence and arousal. So far, results provide a three-dimensional perspective in which the semantic content of a stimulus seemed to have a priority on the affective ones in shaping the structure of emotion.

Ultimately, Study 4 (n=228, *in preparation*) leveraged the unique neuroanatomical and behavioral variability found in semantic dementia, a neurodegenerative disorder characterized by atrophy in the anterior temporal lobes (ATLs), to study the neural correlates of affective and semantic content. Semantic dementia (SD) presents in two clinical forms: those with predominantly left hemisphere atrophy and loss of semantic memory, and those with predominantly right hemisphere atrophy and socioemotional deficits. I reviewed medical records of a cohort of individuals with SD which revealed that those with right-lateralized atrophy showed greater positive emotional

experiences than those with left-lateralized atrophy as well as other changes in behaviors, a pattern I confirmed with structural neuroimaging analyses. This study in a clinical population shed light on the role of the right ATL in binding together semantic knowledge to affective experiences.

In conclusion, behavioral and ERP findings offered valuable insights into the time course of implicit emotion processing emphasizing a critical time window for studying the interplay between semantics and valence. The clinical and neuroimaging findings highlighted the role of the right ATL in socioemotional semantics, opening a new perspective on the mapping of emotions. This research project makes a meaningful contribution to the field by revealing the mechanism through which the brain generates responses tailored to distinct emotions to parse individual emotional experiences.

List of scientific papers

This doctoral thesis is based on the four scientific papers listed below.

1. **L'elaborazione del dolore nel priming affettivo: studio esplorativo** (Study 1)

   Gilioli, A., Borelli, E., & Pesciarelli, F.

   In *Giornale italiano di psicologia* 2023, *50*(1), 37-66.

2. **Electrophysiological correlates of semantic pain processing in the affective priming** (Study 2)

   Gilioli, A., Borelli, E., Serafini, L., & Pesciarelli, F.

   In *Frontiers in Psychology* (2023), *14*, 1201581.

3. **The role of semantic relatedness in predicting the emotion concept organization using an emotion fluency task in older adults** (Study 3)

   Gilioli, A., Zhang, B., Palser, E.R, Gerenza, A., Martinez, A., Morin, B., Roy, A.R, Pillai, J., Vonk, J., Pesciarelli, F., Mandelli, M.L, Gorno-Tempini, M.L, Sturm, V.E.

   In *preparation*

4. **"I'm sending you healing magic": right anterior temporal lobe atrophy relates to elevated positive emotion, mysticism, and religiosity in semantic dementia** (Study 4)

   Gilioli, A., Wallman-Jones, A., Gerenza, A., Palser, E.R, Bogley, R., , Roy, A.R, Pillai, J., Pesciarelli, F., Vonk, J., Ulugut, H., Rankin, K.P, Mandelli, M.L, Perry, D.C, Miller, B.L, Rosen, H.J, Seeley, W.W, Miller, Z.A, Gorno-Tempini, M.L, Sturm, V.E.

   In *preparation*

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Chapter 1

INTRODUCTION

Emotions are traditionally defined as culturally universal, innate, evolutionary ancient processes produced by the subcortical regions of the brain. They enhance survival in critical situations (Kissler, 2013). Emotions result from an appraisal process and are accompanied by changes in experience, expressive behavior, physiological responding, thought, and action (A. S. Cowen & Keltner, 2019).

We learn about emotions through our personal experiences and store language-related emotion concepts as mental representations in the brain. Similar to other semantic concepts, emotion concepts are encoded in the lexicon as semantic memories (Wierzbicka, 1990). Semantic memory typically consists of general factual knowledge about the world, encompassing information acquired throughout the lifespan, such as names and details about objects, historical events, and information related to familiar people (Tulving, 1972). In the case of emotions, the semantics embeds the sensory, motor, and visceral information that gives words and people affective significance (Ralph et al., 2017; Winkielman & Gogolushko, 2018; Zahn et al., 2009). Processing an emotion implies both understanding its meaning (i.e., socioemotional semantic knowledge) and internally simulating the sentiment of that emotion within a particular social context (Decety & Jackson, 2006).

The introduction of the thesis delves into the structure of the semantics of emotions, exploring the affective and semantic variables that shape the semantic space of emotions and examining the underlying neuroanatomical substrates. Lastly, it provides evidence from neuropsychological studies that have probed the impact of brain damage on emotions to investigate the specific role of semantic memory in emotions.

1.1. The semantics of emotions

Despite progress in emotion theory and research, there continues to be ongoing debate about the fundamental nature of emotions. Among the existing theories, the two that have been most discussed are the Basic Emotion Theory (BET) (Ekman, 1992; Izard, 2011; Levenson, 2011; Panksepp, 2011; Panksepp & Watt, 2011) and the Theory of Constructed Emotion (Barrett, 2006a, 2006b, 2017). Other influential, though less popular, theories include those that focus on appraisal (Davidson, 1983).

According to the Basic Emotion Theory, there is a pre-existing set of discrete emotions that have biological differences that can be found in the brain and body. Evidence for this theory has focused on the neurocircuitries (Panksepp, 1998; Panksepp & Watt, 2011), facial expressions (Ekman, 1992), functions (Levenson, 2011), or feelings (Izard, 2011) that characterize each emotion. The key idea is that basic emotions are evolutionarily shaped as they fulfill a purpose in terms of survival allowing an individual to adapt in front of different environmental challenges. They have dedicated universal signals (i.e. face, voice), a distinctive physiology, and a unique function. Paul Ekman posited that there are six basic emotions: happiness, sadness, anger, disgust, fear, and surprise (Ekman, 1992; van Heijst et al., 2023).

In 2017, Barrett L.F. first introduced the Theory of Constructed Emotion, which offers a different viewpoint than BET. This theory suggests that discrete emotion categories are not found in nature but are based on individual experiences and associated with the physical state of the individual and the environment at the time. As a result, emotions are highly dependent on the situation and on our own emotion concepts, which the individual has learned and stored as semantic memories (Barrett, 2017). In appraisal theories, emotions are inextricably tied to differences in the way individuals appraise the environment along several cognitive dimensions, and the deep examination of those dimensions can assist us in understanding not only individual emotions, but also the relationships between them (Smith & Ellsworth, 1985).

Recent studies have suggested that emotions may exist as discrete states within semantic space and linked by gradients. They stated that emotions lie in a multifaceted space that is larger than the six emotions typically studied, and it is also defined by how they are distributed within the space (A. Cowen et al., 2019; A. S. Cowen & Keltner, 2019). The problem of exploring the semantic space of emotion concepts has always been how to map and evaluate fine-grained differences among emotions and how they are represented in different modalities (i.e., face, video, vocalization, words). It appears that categories of emotions do not have clear boundaries but rather unfold within a gradient of combined experiences and manifestations (A. S. Cowen & Keltner, 2019).

The process of experiencing and understanding our own emotions is more complex than just labeling them and relies on multimodal semantic representations (Keltner et al., 2019). According to Bower (1981), human memory can be modeled in terms of an associative network of semantic concepts and schemata that are used to describe events. Evidence for the associative network theory came from studies in which the semantic priming paradigm has been used (Bower, 1981), which demonstrated that people are faster in responding to a *target* stimulus if it is preceded by a *prime* stimulus that is semantically associated. As with any other semantic concept, each emotion concept is represented in memory as a specific node that has connections with other aspects related to that emotion, such as eliciting situations, autonomic reactions, expressive behaviors, or prototypical features. Some of these various associative links are innate, while others are learned and shaped by life experiences. When an emotional stimulus is detected in the environment through an appraisal process, all the information associated with it in the semantic memory network is automatically activated. First, individuals evaluate the emotional value of the stimulus in terms of its positivity or negativity to prepare the appropriate behavioral response of approach or avoidance (Herring et al., 2013; Yao et al., 2019). This primordial ability to categorize stimuli as positive or negative is called *valence*, and it represents an important and universal characteristic of human experience shared across cultures (Lindquist et al., 2016). Research applying the semantic priming paradigm to emotional stimuli (herein affective priming) provided further support to the notion that response to an emotional stimulus is faster when it is preceded by a prime stimulus with the same emotional valence (Fazio et al., 1986). Affective priming studies suggested that positive and negative information are differently organized in memory and elicit distinct behavioral and neural responses (Murphy & Zajonc, 1993)

Historically, several theories have tried to explain the nature of valence. The "bipolarity" hypothesis, elaborated by Wundt (1998), suggested that positivity and negativity lie on the opposite ends of one continuum. This hypothesis has been supported by factor analyses and multidimensional scaling studies of humans' subjective experiences and by studies of how people perceive others' facial movements and vocalizations (Wundt, 1998). More recently, in the mid-twentieth century, a new model called the "bivalence" theory stated that positivity and negativity are independent, and this was also supported by self-report ratings in which individuals used positive and negative labels for the same stimulus. This model views valence as comprising two distinct constructs: one that ranges from positive to neutral, and the other from negative to neutral (Cacioppo et al., 1999; Norris et al., 2010; Watson & Tellegen, 1985).

Although the structure of valence itself remains unresolved, people can react to positive and negative stimuli either with or without engaging the emotional system. When humans perceive the valence of an event, they can respond with an emotional response or with a more cognitive response that reflects their relevant semantic knowledge. For example, when facing a sad situation, one can have a negative emotional experience or, on the contrary, recognize the negativity of the event without necessarily feeling anything (Itkes & Kron, 2019). Researchers defined *affective valence* as the emotional properties that make a stimulus positive or negative, and *semantic valence* as the factual knowledge about the valence of an object or an event (Itkes & Kron, 2019). Both types of valence confer evolutionary advantages. While affective valence benefits the individual by generating autonomic and sensory changes that help them respond to a stimulus, the benefits of semantic valence lie in aiding future behavior planning and interaction with others without being emotionally affected.

Thus, people can classify stimuli according to the valence dimension in a nonexperiential manner, without changes in their feelings, facial expressions, or autonomic activation (Itkes & Kron, 2019).

Further, research showed that stimuli belonging to the same affective domain (positive or negative) but representing different semantic categories (e.g., fear and pain within the negative domain) can elicit specific responses to the conveyed semantic meaning (Rossell & Nobre, 2004). The implication of the double evaluation of affective and semantic valence would differ for positive and negative stimuli, due to the distinct characteristics of positive and negative affect and of their conveyed meaning. Positive emotions share more common features suggesting that they are less categorically differentiated than negative emotions. For instance, a smiling face can be representative of a broad range of positively valenced emotions such as amusement, love, contentment, or joy (Aguado et al., 2013; Campos et al., 2013). Instead, the heterogeneity of semantic contents within the negative domain is more fine-grained likely because their importance in terms of individual survival (Ekman, 1992). A notable example is pain which, despite not traditionally defined as an emotion, embeds a negative affective content that elicits avoidance responses to help individuals moving away from its source and ensure their survival (Van Damme et al., 2008). However, its semantic content also holds a prosocial value that can produce approach responses to help individuals understand and empathize with someone else's pain (Yamada and Decety, 2009). Likewise, anger is a negative emotion that can somehow elicit an avoidance (i.e., withdraw from the situation when anger is experienced) or approach behaviors (i.e., inflict pain to the person that intentionally hurt someone) depending on the situations (Carver & Harmon-Jones, 2009) This highlights the importance of considering both the affective and semantic valence in understanding the different stages of emotional and semantic processing.

The dissociation between affective and semantic valence is pivotal in the ongoing debate about the dimensional structure of the semantic space of emotion. According to the Theory of Constructed Emotion (Russell & Barrett, 1999), emotions can be organized in a circumplex model of semantic space that has two dimensions: valence and arousal (Russell, 1980). Arousal is the degree of activation of a stimulus and is often related to an increase in attention, physiological responses, and behavioral engagement. Despite it represents its own dimension, it is still difficult to separate it from valence. Indeed, stimuli that are assessed as positive or negative usually also produce changes in some level of arousal (Hinojosa et al., 2009; Lindquist et al., 2016; J. Posner et al., 2005; Rohr & Wentura, 2022; Russell, 1979). Traditional models have considered to a lesser extend a third dimension, named dominance, that is conceptualized as the power of the word – a concept can be defined as weak/submissive or strong/dominant (Warriner et al., 2013). Only recently, Itkes & Kron (2019) affirmed the role of a fourth dimension, which shapes the structure of the semantic spaces of affect:

the semantic relationship between concepts. Although the dissociation between affective and semantic representations of valence is challenging, they might be highly correlated and involved in a causal relationship such that semantic knowledge might determine the affective response and, vice versa, the affective experience might color and shape semantic decisions (Itkes & Kron, 2019).

1.2. The representation of semantics of emotions in the healthy brain

Neuroimaging and electrophysiological studies have attempted to explore the representation of emotions in the brain to address questions about the organization of emotional semantics and how the brain distinguishes between positive and negative valence.

1.2.1. Event-related potentials for affective and semantic valence

At an early stage of information processing, the cognitive system automatically evaluates an emotional stimulus in terms of positive or negative valence even before of a deliberate cognitive appraisal of its meaning (Aguado et al., 2013). In literature, event-related potentials (ERPs) provide a high time resolution of milliseconds for recording and analyzing of brain activity that is particularly suited to study the precise time course of rapid and short-lived automatic processes, such as evaluating the affective content of a stimulus. In ERP research, a valuable tool used to measure the automatic evaluation of an emotional stimulus is the affective priming procedure, which implies that the presentation of a prime stimulus can facilitate the elaboration of a target of the same valence (for reviews, Fazio, 2001; Klauer & Musch, 2003). Besides the processing of affective valence, results on affective priming revealed the urge to also consider the processing of its semantic meaning (Aguado et al., 2013; Comesaña et al., 2013). Indeed, several studies showed that the affective and semantic valence are processed at two different stages of stimulus evaluation, and these are reflected by two ERP components, respectively the N400 and the LPP (Aguado et al., 2013; Comesaña et al., 2013).

The N400, as described by Kutas & Hillyard (1980), is a negative deflection that emerges approximately 400 ms after stimulus presentation and it is sensitive to semantic relatedness and congruency. An increased N400 amplitude is typically detected after the presentation of semantically unrelated information between two stimuli (Kutas & Hillyard, 1980). Previous research investigated the effect of the processing of semantic and affective valence on the N400 using an affective priming paradigm (Eder et al., 2012; J. P. Morris et al., 2003; Steinbeis & Koelsch, 2011; Zhang et al., 2010). Although there are still elusive results, most studies have found a greater N400 amplitude in affectively congruent conditions across different stimulus modalities such as words (Herring et al., 2011; J. Morris et al., 2008; J. P. Morris et al., 2003; Zhang et al., 2006), and cross-modal stimuli (face-word in Aguado et al., 2013 ; picture-word in Eder et al., 2012; Zhang et al., 2010; Gibbons et al., 2018). For instance, Schirmer et al. (2002) observed an enhanced N400 when the target word was preceded by an incongruent emotional prosody context. Negative and reverse priming effects have also been detected (Herring et al., 2011; Kissler & Koessler, 2011; Meade et al., 2018; Pan et al., 2016). While the spatial resolution provided by ERPs does not allow for precise localization of the N400, it is usually observed at centro-parietal locations (Gibbons et al., 2018). In addition, evidence from lesions studies, magnetoencephalography, and intracranial recordings suggests that the possible sources of the N400 are located in the temporal areas, specifically in the left superior/middle temporal gyrus, anterior-medial temporal lobe, parahippocampal cortex, and anterior fusiform gyrus (Ibanez et al., 2012)

Another ERP component that appears to be sensitive to the affective and motivational value of stimuli is the late positive potential (LPP), which is a positive deflection peaking at 400-700 ms (Aguado et al., 2013; Ibáñez et al., 2011) and it is responsive to the valence of the stimulus and the preceding emotional context (Schupp et al., 2003). According to several studies, it has a greater amplitude when individuals need to process motivationally relevant stimuli (Schupp et al., 2003), as well as the semantic emotional valence (Cunningham & Zelazo, 2007) and contextual information of stimuli (Cornejo et al., 2009; Hurtado et al., 2009). Similar to the N400, affective priming studies have unveiled an increased LPP amplitude in response to incongruent valence targets across different stimulus modalities such as words (Eder et al., 2012; C. Wu et al., 2021), pictures, and faces (Hartigan & Richards, 2016; Herring et al., 2011; Hietanen & Astikainen, 2013; Li & Lu, 2014; Werheid et al., 2005), and cross-modal stimuli (face-word in Aguado et al., 2013; picture-word in Zhang et al., 2010). It is typically observed at bilateral frontal and parietal locations (Aguado et al., 2013; Werheid et al., 2005), and it has been potentially associated with superior frontal, temporal, and parietal regions (Ibanez et al., 2012).

According to the hierarchical model of affect formulated by Watson & Tellegen (1985), the affective evaluation of a stimulus requires two different levels: the higher hierarchical level regards the affective valence, that is its evaluation in terms of positivity and negativity, while the lower level involves the differentiation among discrete emotional concepts within the same emotional domain (e.g., “irritation” and “rage” belongs to the domain of “anger”) (Aguado et al., 2013). The result of this two-steps evaluation has different implications for positive and negative emotional stimuli; for instance, a smiling face can be easily categorized as a positive emotion because it is a prototypical feature of lots of positive emotions, while a negative facial expression, such as an angry face, can require discriminating between discrete emotional content within the negative domain which is highly challenging. As proof of evidence, the effect of affective congruency on the LPP amplitude has been found even in the absence of N400 effects, indicating that the two components underlie distinct stages of stimulus evaluation (Herring et al., 2011). The LPP appears to be more responsive to affective incongruency, whereas the N400 reflects the semantic content of the stimulus. Therefore, studying these two components can provide insight into the different nature of affective and semantic valence.

1.2.2. The Anterior Temporal Lobe

The temporal pole (BA 38, Planum Polare, area TG, or anterior perirhinal cortex) is a paralimbic region located in the anterior temporal lobe (ATL) that is highly connected with the amygdala, orbitofrontal cortex, temporoparietal junction, and basal forebrain (Olson et al., 2007). Projections from the sensory systems (ventral visual stream, somatosensory, and auditory) to the ATL allows this region to serve as an amodal semantic hub that binds information from different modalities to form domain-general semantic representations. Damage in this region results in gradual loss of semantic memory, applied to both verbal and non-verbal domains (Rogers et al., 2004).

It has been established that the ATL is also crucial for socioemotional processing. Its anatomical connectivity suggests that it is a part of a system that is activated whenever emotions are experienced or imagined, and it is responsible for storing connections between emotions and perceptions as semantic memories (Olson et al., 2007). Lesions to the ATL, frontal cortex, and/or amygdala can lead to noteworthy changes in social behaviors: since these areas share tight connections, they form a network which is commonly referred to as the "social brain" (Brothers, 1990; Frith, 2007). ATL lesions can affect emotion recognition (Macoir et al., 2019) and empathy, key aspects of socioemotional behaviors.

The ATL supports sensory-limbic integration of auditory, visual, and olfactory channels (Olson et al., 2007). The dorsal area of the ATL connects visceral responses to complex auditory signals. Evidence of this comes from neuroimaging studies showing ATL activation for aversive sounds such as a baby crying (Lorberbaum et al., 2002) or a woman screaming (Royet et al., 2000), as well as pleasant sounds such as music (Brown et al., 2004; Platel, 2005; Satoh et al., 2006) and laughter (Royet et al., 2000). The ventral portions of the ATL, in contrast, link visceral responses to complex visual stimuli. PET and fMRI studies have shown ATL activation to both negative and positive visual stimuli, such as videos of cartoons evoking humor reactions, faces, and photographs (for a review see (Olson et al., 2007). There is also some evidence that ATL also responds to olfactory stimuli of differing valences (Royet et al., 2000). Thus, damage to the ATL could result in a decoupling of high-level perception with visceral experiences, which could lead to modality-specific socioemotional disorders (Olson et al., 2007).

Research suggests that the right and left ATL have different specializations (Wong & Gallate, 2012). It has been proposed that the right ATL is the storage unit for personal, episodic memories.

Evidence from fMRI studies has shown right ATL activation for faces and photographs with emotional content (Dolan et al., 2000; Mataix-Cols et al., 2008; Ohira et al., 2006). In contrast, the left ATL is more engaged during tasks involving verbal semantic memory, which is likely due to its proximity to the left-lateralized language areas in the dominant hemisphere (Olson et al., 2007). Neuroimaging findings have also revealed increased left ATL activation when retrieving people's names (Tsukiura et al., 2006, 2011), reading sentences (Ferstl & von Cramon, 2007; Moll et al., 2002; Schaich Borg et al., 2006; Stowe et al., 1999), and completing word tasks (Bright et al., 2004; Diaz & McCarthy, 2009; Ellis et al., 2006; Noppeney & Price, 2002). Taken together, these studies may suggest that while the right ATL is responsible for connecting sensory representations to emotional reactions and social memory, the left ATL links high-level sensory representations, such as faces, to domain-general semantic information. More investigation is required to shed light on the presence of this dissociation (Olson et al., 2007).

Lesion studies and those on neurodegenerative diseases have delved into the role of the ATL in deficits of semantic memory. Historically, studies on temporal lobe epilepsy were crucial to determining the extent to which the right hemisphere is involved in emotions and social behaviors. Several studies have indicated that patients with right lateralized temporal lobe epilepsy have greater rates of psychiatric disorders (Gibbs, 1997; Glosser et al., 2000), hyper-religiosity (Geshwind, 1983; Park, 2005), social and behavioral changes (Lipson et al., 2003). For instance, a study by Lipson et al. (2003) showed that after a right temporal lobectomy, a patient lost emotional attachments to his relatives (Lipson et al., 2003), highlighting the role of the right hemisphere in social behavior and responsiveness (Devinsky, 2000). Additionally, research on patients with traumatic brain injuries supports a right hemispheric dominance for emotional processing within the ATL. Indeed, right brain-damaged patients were more likely to have difficulties classifying and describing feelings compared to left brain-damaged patients (Spalletta et al., 2001). It can also affect social aspects of speech where patients with right frontal lesions had more excessive, disinhibited language colored with embarrassing comments (Alexander et al., 1979; Brownell et al., 1986; Joanette et al., 1990; Weylman et al., 1988).

These findings suggest that the right ATL is responsible for creating a link between perception and emotions and for forming the storage of personal episodic memory, while the left ATL primarily processes semantic and lexical information (Gibbs, 1997). Further research on neurodegenerative disease has proposed a possible lateralization in valence processing within the ATL. A right-sided temporal lobe atrophy was more associated with difficulties in recognizing and expressing negative emotions (Irish et al., 2014; Rosen, 2002), while an enhancement of positive mood and smiling behavior was associated with a left superior temporal lobe atrophy (Shdo et al., 2022; Sturm et al., 2015).

1.2.3. Debate on the hemispheric lateralization of emotions

Neuropsychology has a long history of researching the distinctions between hemispheric asymmetries when it comes to emotional processing. Two competing theories have addressed the issue: the right brain hypothesis (Borod et al., 1998) and the valence hypothesis (Rossi & Rosadini, 1967; Terzian & Cecotto, 1959). The "right brain" hypothesis postulates that the right hemisphere is responsible for the comprehension and expression of emotions. This is based on the evidence that right hemisphere damage has a greater impact compared to left hemisphere damage on both the comprehension and expression of emotions across multiple channels, such as affective prosody and facial expressions (Gainotti, 2019; Ross, 2021). This results in a flattened affect and reduced autonomic responses to emotional stimuli (Ross, 2021).

Functional neuroimaging studies on a healthy population lean more toward a general predominance of the right hemisphere for various facets of emotions. This was reflected by laterality effects on different brain structures related to emotions, such as the amygdala, the anterior insular cortex, the ventromedial prefrontal cortex, and the ATL (Gainotti, 2019). The right hemisphere dominance is not due to a single element of the emotional system, but rather to all components of the right hemisphere emotional network, from the unconscious processing of emotional information in the right amygdala (Morris et al., 1998), to the conscious experience of emotions in the right anterior insula cortex (Craig, 2009; Critchley et al., 2004) , to the representation of emotions and a "top down" control of intense emotional reactions in the right inferior frontal cortex (Aron et al., 2004). These documented asymmetries might explain the right hemisphere's overall dominance for emotions. The right hemisphere relies more on a nonverbal functional organization with a heavier focus on emotional processing sensorimotor information, unconsciousness, and involuntary behavior, while the left hemisphere tends to be more associated with verbal and intellectual activities, consciousness, and purposefulness (Gainotti, 2019).

Others have proposed different models of hemispheric lateralization in emotions. In 1879-81, Jules Bernard Luys noted a difference in emotional behavior between right and left brain-damaged patients: he stated that the right hemisphere is the center of emotions and the left hemisphere the center of intellect (Luys, 1879; 1881). This idea was further explored by Terzian & Cecotto (1959) and Rossi & Rosadini (1967) who observed different emotional behaviors in patients undergoing pharmacological inactivation of the right and left hemispheres. The inactivation of the left hemisphere led to a depressive-catastrophic (negative) behavioral response (crying, pessimism, guilt) and, on the contrary, the inactivation of the right hemisphere led to a euphoric-maniacal (positive) behavior response (laughing, smiling, optimism). Studies conducted in normal subjects using different methodologies supported the hypothesis of different hemispheric specialization: the right hemisphere is involved in the comprehension of negative emotions, and the left hemisphere is involved in the comprehension of positive emotions processing (Ahern & Schwartz, 1979; Natale et al., 1983; P. A. Reuter-Lorenz et al., 1983; P. Reuter-Lorenz & Davidson, 1981). These findings were supported by EEG studies in which brain activity on the left hemisphere was recorded following the visual presentation of positive stimuli, and on the right hemisphere when presenting negative stimuli (Demaree et al., 2005).

More recently, Davidson (1983) looked at the EEG asymmetries in the frontal lobes and confirmed that the left and right frontal lobe responses were not associated with the valence of a stimulus, but rather reflected the approach vs avoidance motivation systems it activates. He reframed the valence hypothesis in terms of “approach vs withdrawal” motivational tendencies. The former is sensitive to reward signals which prompt individuals to engage in approaching behaviors that lead to positive outcomes; the second is sensitive to punishment signals that work to prevent behaviors that may result in negative consequences. In his model, positive approach-related behaviors are associated with the left frontal regions, in particular the left prefrontal cortex, while negative withdrawal-related behaviors are associated with activity in the right frontal region, or right prefrontal (Davidson, 1983).

1.3. Semantic dementia as a model to study hemispheric lateralization of emotions

Frontotemporal dementia (FTD) is a common neurodegenerative condition that leads to dementia before old age, and it encompasses behavioral and personality changes and language deficits associated with frontal and temporal lobe atrophy (Neary et al., 1998). The behavioral variant of frontotemporal dementia (bvFTD) is a subtype of FTD that is characterized by behavioral symptoms (Rascovsky et al., 2011), and the language syndromes include the temporal variant also known as semantic dementia (SD) and the nonfluent variant of primary progressive aphasia (nvfPPA) (Gorno-Tempini et al., 2011). These disorders are due to different levels of neuronal loss and gliosis in the orbitofrontal regions, anterior temporal lobe, or perisylvian language areas.

SD is particularly interesting due to its diverse symptoms that arise in the context of asymmetric atrophy in the frontal and temporal lobes (Borghesani et al., 2020; Seeley et al., 2005). In the early stages of the disease, people may exhibit a linguistic or behavioral clinical presentation (Brambati et al., 2009; Kumfor et al., 2016; Seeley et al., 2005). During its course, the disease gradually extends to the opposite hemisphere resulting in the co-occurrence of language and behavioral disorders. Given that both left anterior temporal lobe and right anterior temporal lobe predominant degenerations are usually linked to frontotemporal lobar degeneration-transactive response DNA binding protein 43 type C (FTLD-TDP type C) pathology (Borghesani et al., 2020), the asymmetric lateralization of the ATL results in distinct clinical manifestations along a unified pathological continuum (Seeley et al., 2005; Snowden et al., 2018; Younes et al., 2022).

In general, SD is defined by a profound loss of conceptual knowledge with relative preservation of other cognitive abilities. SD encompasses two distinct syndromes with specific symptomatic and cognitive profiles that, however, share some core features (Thompson et al., 2003). On one hand, left-lateralized atrophy of ATL results in predominant language deficits and a significant loss of verbal and object-related semantic knowledge (Hodges et al., 1992; Mummery et al., 2000). This syndrome was defined by Gorno-Tempini et al. (2011) as a semantic variant primary progressive aphasia (svPPA) and it implies a disruption of the core semantic representation manifested as word-finding difficulties (anomia), poor single-word-comprehension and object-identification impairments in a variety of semantic tasks irrespective to the modality of testing. The definition of svPPA syndrome helped to state the unique contribution of the left ATL in the representation of language (Ralph et al., 2001).

On the contrary, damage to the right ATL leads to loss of person specific knowledge (i.e., poor familiar faces recognition), deficits in a wide range of socioemotional functions including empathy (i.e., labeling emotions; paralinguistic cue detection and facial emotion recognition), and profound changes in emotions and behavior (Binney et al., 2016; D. Chan et al., 2009; Edwards-Lee, 1997; Gorno-Tempini et al., 2004; Henry et al., 2014; Josephs et al., 2009; Perry et al., 2001). This has been recently described as a semantic variant of FTD (sbvFTD) by Younes et al. (2022) and implies a potential loss of semantic knowledge for socioemotional concepts (Younes et al., 2022) highlighting the significance of the right ATL as the core hub for socioemotional semantic knowledge (Olson et al., 2007; Younes et al., 2022).

It has been well recognized that in patients with svPPA and left ATL atrophy, the loss of semantic knowledge for objects hinders a patient's ability to connect verbal semantic features to words and people, and to retrieve and articulate words and names (Bozeat et al., 2000; Hodges et al., 1992; Mummery et al., 2000). Instead, it is not fully clear the nature of the impairments in patients with sbvFTD. Patients with sbvFTD typically show less severe verbal semantic deficits than those with svPPA but have more behavioral symptoms including loss of emotional empathy (Multani et al., 2017; Rankin et al., 2005) and decreased recognition of people and emotions (Irish et al., 2014; Snowden et al., 2001; Ulugut Erkoyun et al., 2020). In sbvFTD, the primary area of impairment is socioemotional semantic knowledge which encompasses the sensory, motor, and visceral information that infuses the affective significance to words and people (Seeley et al., 2012). Changes in behavior and emotions such as lack of empathy, deficits in emotion perception, reactivity, and experience may arise because patients lack access to visceral cues that foster feelings of familiarity and affect-sharing (Zahn et al., 2009). The sbvFTD variant provides an exclusive opportunity to understand the nature of the semantics of emotions and how lateralized anterior temporal damage relates to alterations of the processing of emotion and valence.

Despite the prominent impairment in socioemotional knowledge occurring in sbvFTD supports the right dominance hypothesis for emotions, deficits in emotion recognition also occurred in svPPA across different modalities, such as facial expression (Kumfor et al., 2011; L. A. Miller et al., 2012), musical stimuli (Hsieh, Hornberger, et al., 2012), and emotional words (Hsieh, Foxe, et al., 2012). The mechanism behind these deficits is still unclear. Few studies showed a specific deficit in recognition of negative emotions associated with a right-sided atrophy (Irish et al., 2013; Rosen, 2002) leaning towards a hemispheric lateralization for the processing of valence. Additionally, patients with right-sided atrophy frequently experienced feelings of connectedness with the natural and supernatural world together with elevated positive mood and lack of empathy towards other human beings (Ohm et al., 2023; Perry et al., 2001; Rankin et al., 2006; Rosen, 2002; Vonk et al., 2020). These combinations of changes prompted a loss of reaction to negative emotions and a gain of experience of positive ones. In contrast, recent studies have also found an increased positive emotion reactivity in people with svPPA associated with greater atrophy of the left hemisphere (Shdo et al., 2022; Sturm et al., 2015) leaving open the debate.

SD represents a unique model to elucidate the peculiar nature of the semantics of emotions and the hemispheric involvement in the processing of emotions and valence (Bozeat et al., 2000; Gainotti, 2019; Snowden et al., 2001). This population might represent a key to unlock the ongoing debate on the neural representation of emotions and valence.

THE PRESENT THESIS

This thesis examines the organization of emotion content in semantic memory using a multimodal approach that includes studies of healthy populations and people with semantic dementia. Posner (1975) postulated that two cognitive processes are involved in accessing and retrieving semantic information: the first is automatic and it occurs during the perception of the stimulus; the second is controlled and effortful, involving a search through semantic memory for the appropriate stored units that may not have been activated in the initial and automatic spread of activation (Posner, 1975). For this reason, I decided to use two different tasks to study the structure of the semantics of emotions: the affective priming, which implies an automatic level activation of semantic information, and the emotion fluency task, which requires mechanisms of controlled access to semantic memory.

Studies 1 and 2 used an affective priming paradigm to study the interaction of the affective and semantic content of emotional word stimuli in healthy individuals. I decided to use pain as a model because it embeds a negative affective content with specific semantic properties that confers it an evolutionary value. Indeed, the semantics of pain might elicit both avoidance (i.e. escape from threats) or approaching behaviors (i.e. empathic responses). In this paradigm, I investigated whether participants were faster in evaluating a negative word when it was preceded by a negative word related or not related to pain. In Study 1, I recorded behavioral responses and hypothesized an affective priming effect where participants had faster reaction times and higher accuracy scores when negative target words were preceded by pain prime words. This would suggest the evolutionary role of pain in preserving the survival of the individuals by promptly reacting to pain stimuli. In Study 2, I recorded event-related potentials (ERPs) in EEG activity to elucidate the temporal course of the affective and semantic processing, which supports the idea that the affective and semantic contents are elaborated at different stages of processing reflected by two different ERP components, respectively N400 and LPP.

Study 3 used an emotion fluency task to investigate the organization of emotion concepts in semantic memory according to their valence, semantic relatedness, and arousal. The goal of this study was to investigate if the valence of the words influences the retrieval of emotional words during a voluntary task, as proof of the storage advantages of positive or negative socioemotional concepts in the semantic memory. It also proposed to test if valence, arousal, and semantic relatedness are significant predictors of the order of production of emotion words.

Finally, Study 4 aimed at shedding light on the lateralized contribution of the anterior temporal lobe to socioemotional knowledge by studying the behavioral and emotional changes in a group of people with semantic dementia. People with right-sided atrophy might lose the ability to link the word of an emotion with the feeling attached to that emotional word, resulting in a reduced understanding of emotions and a general loss of empathy. This is particularly evident for negative emotional concepts, which may lead to experience a feeling of connectedness to the world and an increased sense of positivity, frequently reported by these individuals.

The entire manuscript delves into the ongoing debate regarding the hemispheric lateralization of socioemotional semantic knowledge in the brain. The behavioral and EEG studies are crucial for addressing this issue at a perceptual level using a paradigm grounded in automatic processes. Emotion fluency is a sensible tool for understanding how individuals consciously parse their emotional experiences in semantic memory. Lastly, the study of semantic dementia and its phenotypes sheds light on the brain correlates of emotion dysregulation and dysfunctions. The narrative of these four studies aims to uncover the unique nature of the semantics of emotions by studying its temporal and spatial correlates in the brain.

Chapter 2

Pain processing in affective priming: an exploratory study

2.1. Introduction

Beyond the affective content of a stimulus, its semantic content also has a role in modulating the attentional system. Affective and semantic contents refer to different and independent dimensions of stimuli and, while the role of the former in modulating cognitive responses is well established, only recently has it been proposed that the latter may also play a part (Lindquist et al., 2016).

Stimuli semantically associated with pain, like words conveying pain or faces expressing pain, usually hold a negative affective content. Yet, a semantic content associated with pain is more salient compared to other negative semantic contents. This is likely because of its relevance for the well-being and survival of the individual (Aguado et al., 2018; J. A. Brooks et al., 2017; Kveraga et al., 2015; Yao et al., 2019), which makes the stimulus processing more urgent compared to other negative stimuli with different, less salient, semantic contents. Although pain is usually not considered an emotion, it can be defined as an unpleasant emotional and sensory experience (Raja et al., 2020), which gives it an extremely negative valence (Borelli et al., 2018, 2021). This can be true in the case of real pain as well as potential pain or pain threat. Regardless, pain threat may represent a signal that individuals have to move away to protect themselves and to promote their own survival. By virtue of its evolutionary function, it must be detected by the cognitive system with priority with respect to other stimuli (Yamada & Decety, 2009).

However, pain also holds a pro-social value when it implies an approach response toward someone else in pain (Yamada & Decety, 2009). A review by Betti and Aglioti (2016) reported numerous studies in agreement that observing individuals expressing or experiencing pain activates the same brain areas involved in the physical experience of pain itself, generating a sensory, perceptive, and behavioral simulation as a first-hand pain experience (Borelli et al., 2018).

Not only the attention but also the behavioral response to the stimulus seems to be guided by valence (Mouras & Lelard, 2021). Based on the motivational priming theory (Davidson & Irwin, 1999; P. J. Lang, 1995; LeDoux, 2000), emotions prime two motivational systems which guide behaviors: the aversive system, which facilitates avoidance/withdrawal responses towards negative stimuli, and the appetitive system, which promotes approaching responses towards positive stimuli (Bradley et al., 2001; Horslen & Carpenter, 2011; P. Lang & Bradley, 2007; P. J. Lang et al., 2000, 2005). The activation of these two motivational systems seems to produce subjective responses to emotions; on the contrary, their impairment may result in emotional deficits. On one hand, valence defines which of the two systems activates; on the other hand, arousal seems to determine the intensity of activation (Rhudy & Williams, 2005). In this regard, the affective context in which a stimulus is embedded plays a critical role in its processing. When the aversive system is pre-activated by negative emotional stimuli present in the environment, it can indeed be facilitated in the generation of avoidance behaviors; on the contrary, it can be inhibited if pre-activated by positive ones (Meagher et al., 2001).

In the literature, an experimental paradigm massively used to investigate how the affective context automatically affects the evaluation of the stimulus in terms of positivity or negativity is the affective priming (Gibbons et al., 2018; Hu & Liu, 2019). Affective priming refers to the influence of emotionally charged stimuli on subsequent evaluations or reactions. According to this paradigm, the elaboration of a first stimulus (prime) may facilitate or inhibit the subsequent behavioral response to a second stimulus (target) if the two stimuli are congruent or incongruent, respectively, in terms of valence (e.g., prime HOLIDAY - target TRIUMPH vs prime JOYFUL - target STINK).

In agreement with the spreading activation theory (Fazio et al., 1986; Murphy & Zajonc, 1993), the priming effect is due to the fact that the valence of the prime pre-activates the network of concepts associated with it, facilitating the subsequent processing of the target if its affective meaning is represented in this network of concepts, through a mechanism similar to one underlying the semantic priming (Neely, 1991). This agrees with the motivational priming theory: when the aversive system is pre-activated by negative stimuli, the individual will be facilitated in implementing avoidance behaviors. On the contrary, this avoidance response will be inhibited when the appetitive system is pre-activated by positive stimuli (an incongruent condition between prime and target).

Although the affective congruency effect, named priming effect, seems to be consistent for positive valence stimuli (Aguado et al., 2013; Contreras-Huerta et al., 2013; Gibbons et al., 2014), results are not coherent as regarding negative stimuli. It is not clear whether the negative valence information facilitates (Meng et al., 2013; Paulmann & Pell, 2010) or inhibits (Song et al., 2019; C. Wu et al., 2021) the processing of subsequent negative stimuli. It is possible to speculate that this inconsistency in results is because the negative valence of stimuli, in determining their priority, interacts with their semantic content generating emotion-specific responses (Fazio et al., 1986). According to this hypothesis, negative valence would thus constitute a heterogeneous domain that, if treated as a single semantic category, would lead to incongruent data. For example, the semantic content associated with pain could have properties relevant to its fundamental role in the well- being and integrity of the organism (Aguado et al., 2018; J. A. Brooks et al., 2017; Kveraga et al., 2015; Yao et al., 2019), making its processing more urgent than other negative domains (e.g., anger and fear). By virtue of its developmental function, it must be detected by the cognitive system in priority to other stimuli (Yamada & Decety, 2009). Therefore, pain represents a suitable model for understanding whether the specificity of the semantic content of the affective context interacts with valence in modulating the subsequent processing of positive or negative stimuli.

So far, only a few studies demonstrated that the semantics of pain embedded in pictures (Cameron et al., 2017; Meng et al., 2013), faces (Burton et al., 2005; Chiesa et al., 2015, 2017), and words (Grynberg & Maurage, 2014; Meconi et al., 2018; Richter et al., 2014; Swannell et al., 2016; Yamada & Decety, 2009) can be processed in an automatic and early way to the point of influencing the response to subsequent pain stimuli. According to the motivational priming theory, the negative emotional information contained in a stimulus can pre-activate the aversive system and enhance both the physiological and behavioral response to a following pain stimulus (Cameron et al., 2017; Grynberg & Maurage, 2014; Meconi et al., 2018; Meng et al., 2013; Richter et al., 2014; Swannell et al., 2016; Yamada & Decety, 2009). This means that, due to its aversive nature, the individual will rapidly respond to a pain stimulus when previously exposed to negative information rather than positive one (Yamada & Decety, 2009). A study by Yamada and Decety (2009) showed how implicit processing of information with negative content would facilitate the tendency to evaluate the intensity of pain in others. These responses would even be more intense in females than in males: according to a substantial number of studies, females would be more sensitive to negative stimuli by showing more intense reactions to pain (Bradley et al., 2001; Rhudy & Williams, 2005). Nevertheless, there is little evidence that showed a reverse effect reporting that the processing of a negative prime might also inhibit the subsequent elaboration of a pain stimulus (Burton et al., 2005; Song et al., 2019).

The present study, therefore, represents a first attempt to explore how the processing of the valence and semantic content of stimuli associated with pain can influence the subsequent processing of a negative valence stimulus. To avoid the inherent ambivalence of faces associated with pain, it was decided to use only words as stimuli. Using two experiments, we investigated how negative stimuli are processed differently based on their semantic content, depending on whether they are associated with the semantic of pain or not.

2.2. EXPERIMENT 1

In Experiment 1, affective priming was used to investigate how the processing of a first word (prime) stimulus associated with pain can either facilitate or inhibit the subsequent behavioral response to a second word (target) stimulus with negative valence. For this purpose, we used positive and negative prime stimuli (associated and not associated with pain) and positive and negative valence target stimuli (not associated with pain). To analyze the influence that the prime has on the target, the reaction times (RTs) and accuracy scores of the participant, who had to decide whether the target stimulus was a positive or negative word, were recorded.

First, it was expected that an affective priming effect would emerge when the prime and target had positive valence, going to confirm what was already present in studies on affective priming. This would mean that in the condition of affective congruence between prime and target, the participant tends to respond faster and more accurately than in the affective incongruent condition (negative prime - positive target). On the other hand, for negative valence stimuli, in the literature studies are still debating. If a negative prime facilitated the subsequent processing of a negative target, a priming effect was expected in the congruent condition between the prime and target. On the contrary, if the processing of a negative prime inhibited the response to a negative target, no priming effect was expected for reaction times and accuracy scores in the congruent condition.

In accordance with the motivational priming theory, pain revests a key role in the survival of the organism. Thus, stimuli associated with pain can potentially intensify the perception of negative stimuli present in the environment to preserve the integrity of the individual (Meagher et al., 2001). Therefore, Experiment 1 aimed foremost to replicate the priming effect for positive stimuli highlighted in the literature and, more importantly, to investigate the role of the semantic of pain in the processing of negative stimuli so that the conflicting data on negative priming in the literature could be clarified.

2.2.1 Methods

2.2.1.1. Participants

Twenty-seven students (12 females, 15 males) from the University of Modena and Reggio Emilia aged 18 to 27 years participated in the present study. The participants were all healthy volunteers, native Italian speakers, with normal or lens-corrected vision. The presence of neurological and/or psychiatric disorders was a reason for exclusion from the study. Two participants were excluded from the analysis due to errors in the methodological procedure: in the first case, the experimenter accidentally stopped the trial at the end of the third block; in the second case, the experiment was interrupted by a system update. Analyses were thus conducted on 25 participants, including 12 females and 13 males.

The sample size was established based on heuristic evaluations of the affective priming literature, which reports numerous studies with samples of 22-33 participants (Wu et al., 2021; Yamada & Decety, 2009). We also conducted a posteriori *sensitivity power analysis* (Lakens, 2022) according to which, given $N = 25$, $a = .05$ and a *power* of 80%, we found a minimum *partial* η^2 of .27, consistent with the literature on the subject.

This study was carried out in accordance with the recommendations of the "Italian Association of Psychology" (AIP) Ethical Guidelines (Codice Etico: www.aipass.org/node/11560), and was approved by the local Ethical Committee of the University of Modena and Reggio Emilia. All participants gave written informed consent in accordance with the Declaration of Helsinki and they voluntary enrolled in the experiment.

2.2.1.2. Stimuli

Overall, 256 Italian words (both adjectives and nouns) were adopted for this study, among which 32 negative words associated with pain (henceforth, pain words; e.g., *ferita*, injury;), 96 negative words not associated with pain (henceforth, negative words; e.g., *vandalo*, vandal), and 128 positive words (e.g., *vita*, life) (for the complete word list and English translation, see Supplementary Table 1). Positive and negative words were selected from the Italian version of the ANEW database (Affective Norms for English Words; (Montefinese et al., 2014), while pain words were selected from the WOP database (Words of Pain, WOP; (Borelli et al., 2018). Pain words were chosen based on their pain-relatedness scores (Borelli et al., 2018), which had to be in the range between 6 and 7 on a rating scale from 1 (not at all associated with pain) to 7 (extremely associated with pain). The three categories of words were controlled for the main psycholinguistic and affective variables that are known to affect the time it takes to process a word, namely familiarity, length in letters, valence, and arousal (see Table 1 for descriptive statistics). Each prime-target pair was also controlled for semantic relatedness (Pedersen et al., 2004).

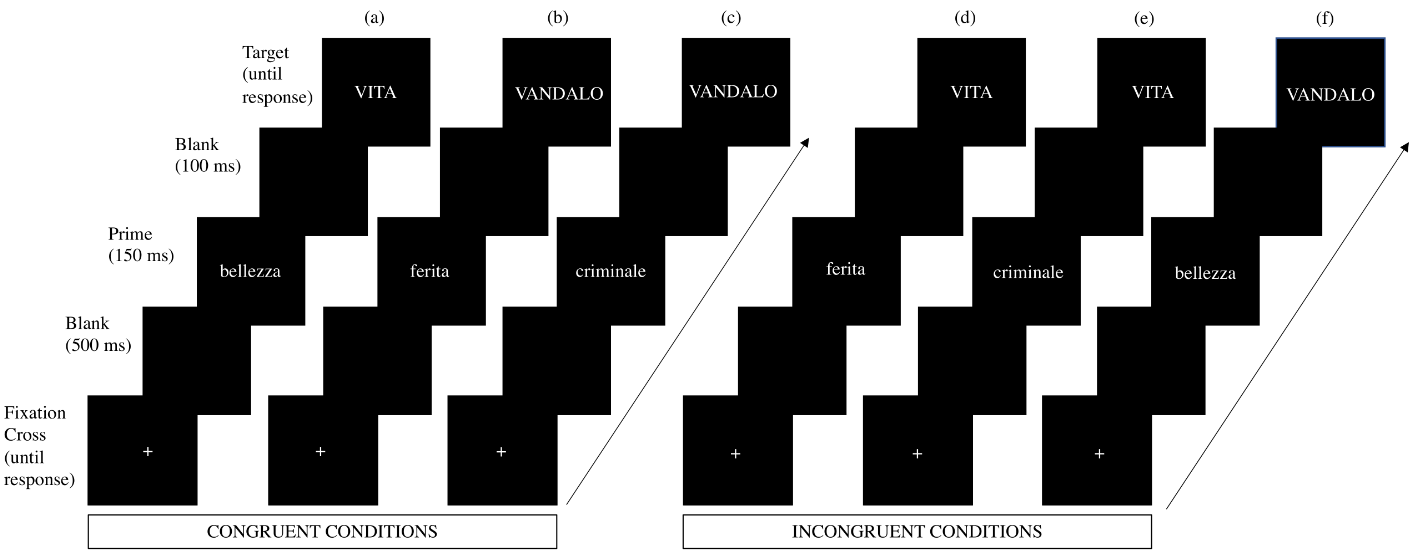
The 256 words were divided into 128 prime stimuli and 128 target stimuli. Prime stimuli included 32 negative words/prime, 32 pain words/prime, and 64 positive words/prime, whereas target stimuli comprised the remaining 64 negative words/target and the remaining 64 positive words/target. Both prime words and target words were presented 4 times during the entire experiment in 4 blocks and paired to form 512 prime - target pairs (see Figure 1). Thereby, we obtained 256 congruent pairs (128 positive prime - positive target; 64 pain prime – negative target; 64 negative prime – negative target), and 256 incongruent pairs (128 positive prime - negative target; 64 negative prime - positive target; 64 pain prime - positive target).

Participants performed four blocks. Within each block, a list of 128 out of 512 prime-target pairs was presented each in a separate trial in a randomized order. The lists were randomized among participants.

Table 1. Descriptive statistics of familiarity, length in letters, valence, and arousal for the three categories of words (i.e., positive, negative, and pain stimuli).

		Familiarity M (SD)	Valence M (SD)	Arousal M (SD)	Length M (SD)
Prime	Positive words	5.05 (±0.46)	5.99 (±0.32)	4.85 (±0.63)	7.44 (±2.11)
	Negative words	4.71 (±0.74)	1.83 (±0.24)	5.06 (±0.50)	8.34 (±1.7)
	Pain words	4.71 (±1.13)	1.67 (±0.39)	5.25 (±0.7)	8.44 (±2.37)
Target	Positive words	5.05 (±0.58)	5.97 (±0.30)	5.06 (±0.45)	7.47 (±1.97)
	Negative words	4.76 (± 0.6)	1.85 (±0.23)	4.82 (±0.60)	7.77 (±1.72)

Figure 1. Time sequence of events during an illustrative (a) positive prime – positive target trial, (b) pain prime – negative target trial, (c) negative prime – negative target trial, (d) pain prime – positive target trial, (e) negative prime – positive target trial, and (f) positive prime – negative target trial. The illustrative trials a, b, and c represent the congruent condition, and the illustrative trials d, e, and f represent the incongruent condition. Briefly, a fixation cross (+) was displayed on the screen. Once participants pressed the start button, they were presented in this order with a blank for 500 ms, the prime stimulus for 150 ms, another blank for 100 ms, and the target stimulus, which remained on the screen until the participants' response. Participants were instructed to evaluate the valence of the target stimulus and to press a button if positive or another button if negative.



2.2.1.3. Procedure

The experiment was implemented in E-prime software (Version 3; Psychology Software Tools, Pittsburgh, PA) and was presented as a study on how people categorize stimuli based on their positive or negative valence. All stimuli were presented in the center of a 17 CRT monitor synchronous with the screen refresh [Philips 107B; refresh rate =60 Hz (16.67 ms)] that was positioned at eye level approximately 70 cm in front of the participant, such that each stimulus subtended 1.2-4.1° of horizontal visual angle and 0.5° of vertical visual angle. As shown in Figure 1, each trial began with a fixation cross (+) presented for 800 ms in the middle of the screen. Then a black screen (blank) was displayed for 500 ms and replaced by a prime stimulus lasting 150 ms, followed by another blank lasting 100 ms. Once the blank disappeared, a target stimulus appeared for 1500 ms. The primes and the targets were presented in the center of the screen in white lowercase letters for the former and in uppercase letters for the latter (20-point Calibri bold font) on a black background. The interstimulus interval was set up at 1000 ms after the participant's response. Participants were instructed to evaluate, as quickly and accurately as possible, whether the target was a positive or negative word (valence judgment task) and to respond by pressing one of two buttons, which were counterbalanced (left and right) across participants. Participants performed a practice session consisting of 8 trials (half congruent pairs and half incongruent pairs) prior to study onset to ensure that they understood the task. Stimuli in the practice session were different from the experimental ones.

2.2.1.4. Questionnaires

To assess for individual differences in pain processing, we administered three questionnaires at the end of each experimental procedure: the Italian version of Behavioral Approach/Inhibition System Scale (BIS/BAS scale) (Leone et al., 2002) which evaluates the activation and inhibition system; the Italian version of Pain Catastrophizing Scale (PCS-I, (Monticone et al., 2012) which measures the individual disposition in pain anxiety and catastrophizing; and the Italian version of the Interpersonal Reactivity Index (IRI,(Albiero et al., 2006) which is a measure the dispositional response empathy by integrating affective and cognitive components (e.g., perspective taking, personal distress).

2.2.1.5. Statistical Analyses

Statistical analyses were performed using JASP software (JASP Team,2022 Version 0.16.3). The analysis of accuracy scores was initially performed. RTs and ERP analyses were then carried out on trials with correct responses. Individual RTs exceeding ± 2 standard deviations (SD) were excluded from the analysis.

To investigate the role of the prime valence, we performed repeated-measures 2x2X2 ANOVAs on the accuracy scores and the mean RTs with prime valence (positive, negative) and target valence (positive, negative) as within-subject factors and the gender of participants (males, females) as a between-subject factor. To examine significant interactions, we performed planned paired samples t-tests based on a-priori hypotheses.

Then, to investigate the role of the semantic content of negative prime, we performed repeated-measures 3x2X2 ANOVAs on the accuracy scores and the mean RTs with prime semantics (positive, negative, pain) and target valence (positive, negative) as within-subject factors and the gender of participants (males, females) as a between-subject factor. To examine significant interactions, we performed planned paired samples t-tests based on a-priori hypotheses. In the 3x2x2 ANOVAs on prime semantics, 64 positive words were compared to negative words, of which 32 were unrelated to pain and 32 were related to pain. For this reason, this analysis resulted in not having the same power as the 2x2x2 ANOVA on prime valence and some effects detected in the latter might appear to weaken in the former. For this reason, both ANOVAs are meaningful to the aim of the study.

To account for violations of sphericity, the Greenhouse–Geisser procedure was used to correct degrees of freedom: only corrected significance levels are reported. The level of significance for all statistical analyses was set to $p<.05$.

To test the influence of individual differences in pain processing on RT effects, we performed Spearman's correlations between the scores in the questionnaires' subscales and the RTs differences between congruent and incongruent pairs.

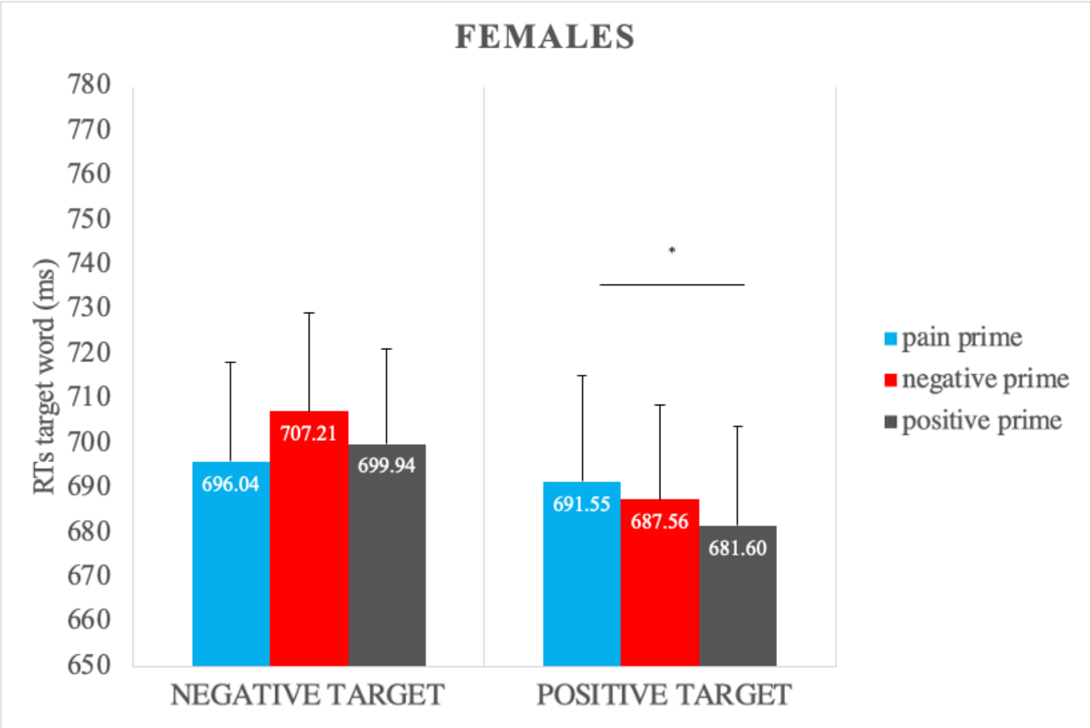
2.2.2. Results

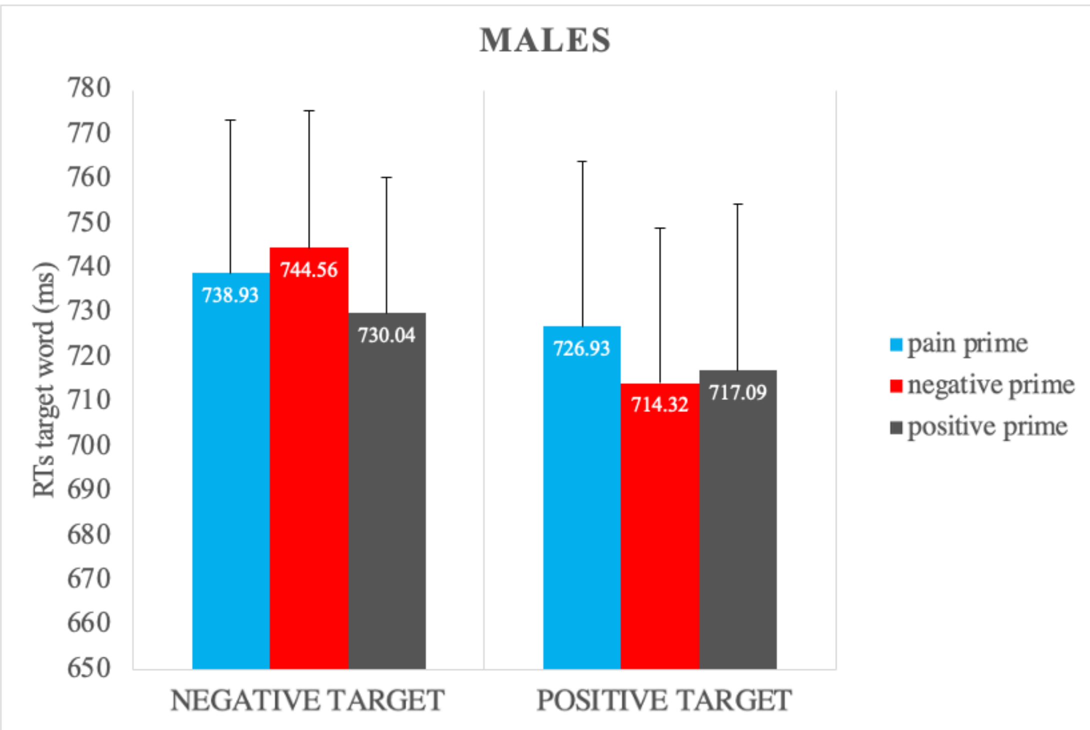
9.4% of the trials were excluded from the analyses because the RTs exceeded ± 2 *SD*. For accuracy scores, the 2 × 2 × 2 ANOVA showed no significant effects (*ps* > .05). For RTs, the two main effects for prime valence [F (1, 23) = 7.895, p = .010, η_p^2 =.256] and target valence [F (1, 23) = 7.138, p = .014, η_p^2 = .237] were significant. Positive primes were elaborated faster than negative ones regardless of the valence of the target. Similarly, positive targets were elaborated faster than negative targets regardless of the valence of the prime. However, the prime valence x target valence interaction was not significant for either accuracy scores or RTs. Contrary to what was hypothesized, no priming effect emerged in the congruence conditions (positive prime- positive target; negative prime-negative target) (*ps* > .05).

Next, to test whether the pain prime could elicit a priming effect, a 3 × 2 × 2 ANOVA was performed. The analysis on accuracy scores showed no significant effects (*ps* > .05). Whereas the analysis on RTs showed a main effect of target valence [F (1, 23) = 6.897, p = .015, η_p^2 = .231], so that the positive target was elaborated faster than the negative target regardless of the valence of the prime. The analysis on RTs also revealed two marginally significant effects: a main effect of prime valence [F (1.8, 23) = 2.693, p =.086, η_p^2 = .105] so that positive primes were processed faster than the negative and the pain ones, and a priming effect represented by prime semantics x target valence interaction [F (1.8, 41.3) = 2.989, p =.067, hp^2 = .115]. To further examine this interaction, paired-sample t-tests showed significantly faster RTs when the positive target was preceded by positive primes than a pain prime [t (24) = -2.485, p = .01, Cohen's d = -.497], confirming the hypothesis.

In both ANOVAs, gender of participants was not a significant variable (p > .05). Nevertheless, the descriptive analysis revealed differences in RTs between females and males, which were further investigated by paired-samples t-tests on the mean accuracy scores and RTs. The statistics showed that females had faster RTs than males in the condition in which the positive target was preceded by a positive prime rather than a pain prime [t (11) = -1.846, p = .046, Cohen's d = -.533] (Figure 2). No significant correlation was found for the scores on each of the subscales of the questionnaires.

Figure 2. Gender differences in affective priming (significant comparison highlighting the priming effect for the positive target is indicated with an asterisk).





2.2.3. Discussion Experiment 1

The main purpose of Experiment 1 was to investigate the effect that the processing of pain words has on the subsequent processing of a negative stimulus. To study this effect, we employed an affective priming paradigm which has been widely utilized in the literature to study automatic processes, such as the implicit processing of negative information. To date, it has never been used with pain word stimuli.

An initial analysis revealed no affective priming effects in the congruence condition for both positive and negative valence. In a subsequent analysis, the introduction of the semantic of pain associated with a negative prime revealed a marginally significant interaction between the prime valence and target valence, indicating that the positive target was elaborated faster when preceded by a positive prime than a pain prime. This effect, while modest, is consistent with previous research on affective priming. A review by Yao et al. (2019) showed that valence has a strong contribution in affective priming, especially positive valence information contained in prime stimuli can significantly increases the accessibility and processing of positive targets. Interestingly, the priming effect for positive stimuli emerged when pain semantics associated with a negative prime was introduced into the analysis: the difference between the congruent condition (positive prime- positive target) and the incongruent one (pain prime- positive target) was significant when the negative prime was distinguished for the semantics of pain. This suggests that negative stimuli can be represented by different emotional categories (i.e., pain, anger, or fear), which can play a specific role in the affective priming paradigm (Aguado et al., 2018).

In contrast, the literature remains unclear about whether the response to negative stimuli is facilitated or inhibited by the implicit processing of negative primes, particularly when associated with pain. It is challenging to determine whether the absence of affective priming for negative stimuli in our experiment lies in the experimental paradigm or, rather, can be attributed to the fact that the negative valence and the semantics of pain do not generate this effect. Since a clear priming effect for positive stimuli did not emerge in Experiment 1, which appears to be very consistent in the literature (Aguado et al., 2013; Contreras-Huerta et al., 2013; Gibbons et al., 2014), it is reasonable to look for the possible cause in the experimental paradigm used.

As previously shown by Fazio et al. (1986), a moderating variable of affective priming effects is the time between the presentation of the prime and the target onset, also referred to as *stimulus onset asynchrony* (SOA). In the present experiment, the SOA was set at 250 ms because numerous studies that manipulated this parameter have shown that affective priming was present at SOAs less than or equal to 300 ms (Fazio et al., 1986; Greenwald et al., 1995; Klauer, 1997) and not at longer intervals (Hermans et al., 1996; Klauer, 1997). Therefore, it is possible that this variable may have influenced the results.

Additionally, the data from the present experiment suggested gender differences among participants (Figure 2): indeed, female reported faster RTs in the affective congruent condition when positive target was preceded by a positive prime rather than a pain prime. This result agreed with numerous studies which reported gender differences in emotion processing (for a review see Rhudy & Williams, 2005). Females usually perform better on emotional tasks than males, showing greater sensitivity to the emotional component of stimuli in the environment (Yamada & Decety, 2009).

To further consider these factors that may have influenced the emergence of the priming effect with word stimuli, a second experiment was conducted in which these two variables were included.

2.3. EXPERIMENT 2

Taking into consideration the results of Experiment 1 and the literature on affective priming, a second experiment was conducted only on a female sample, in which the SOA was modified. Since most studies on affective priming detected the emergence of this effect at SOA equal to 300 ms (Aguado et al., 2013; E. Chan et al., 2006; Fazio et al., 1986), in the present experiment we used a SOA of 300 ms instead of 250 ms as in Experiment 1. Considering that Experiment 1 revealed a tendency towards affective priming for positive stimuli in female participants, the present experiment focused solely on a sample of female participants.

Experiment 2 aimed to replicate the affective priming effect for positive stimuli as previously demonstrated in the literature. Moreover, it aimed to clarify the conflicting data regarding priming for negative stimuli. We were interested in investigating the role of pain in the processing of negative stimuli to determine whether the pain information associated with the prime stimulus can influence the processing of the subsequent negative target stimulus.

2.3.1. Methods

2.3.1.1. Participants

The participants in the present study are 31 female students at the University of Modena and Reggio Emilia with ages ranging from 18 to 23 years. The participants are all healthy volunteers, native Italian speakers, with normal or lens-corrected vision. The presence of neurological and/or psychiatric disorders is a criterion for exclusion from the study. A student was excluded from the study because she learned of the purpose of the experiment before the task was performed. Analyses were then conducted on 30 female participants.

2.3.1.2. Stimuli

The stimuli and experimental conditions are the same as those presented for Experiment 1.

2.3.1.3. Procedure

The procedure is the same as that used in Experiment 1 in which, however, the SOA was changed from 250 ms to 300 ms, extending the prime presentation from 150 ms to 200 ms. In addition, the target duration was set so that it remained on the screen until the participant's response.

2.3.1.4. Questionnaires

The questionnaires administered to the participants are the same as those used in Experiment 1.

2.3.1.5. Statistical analyses

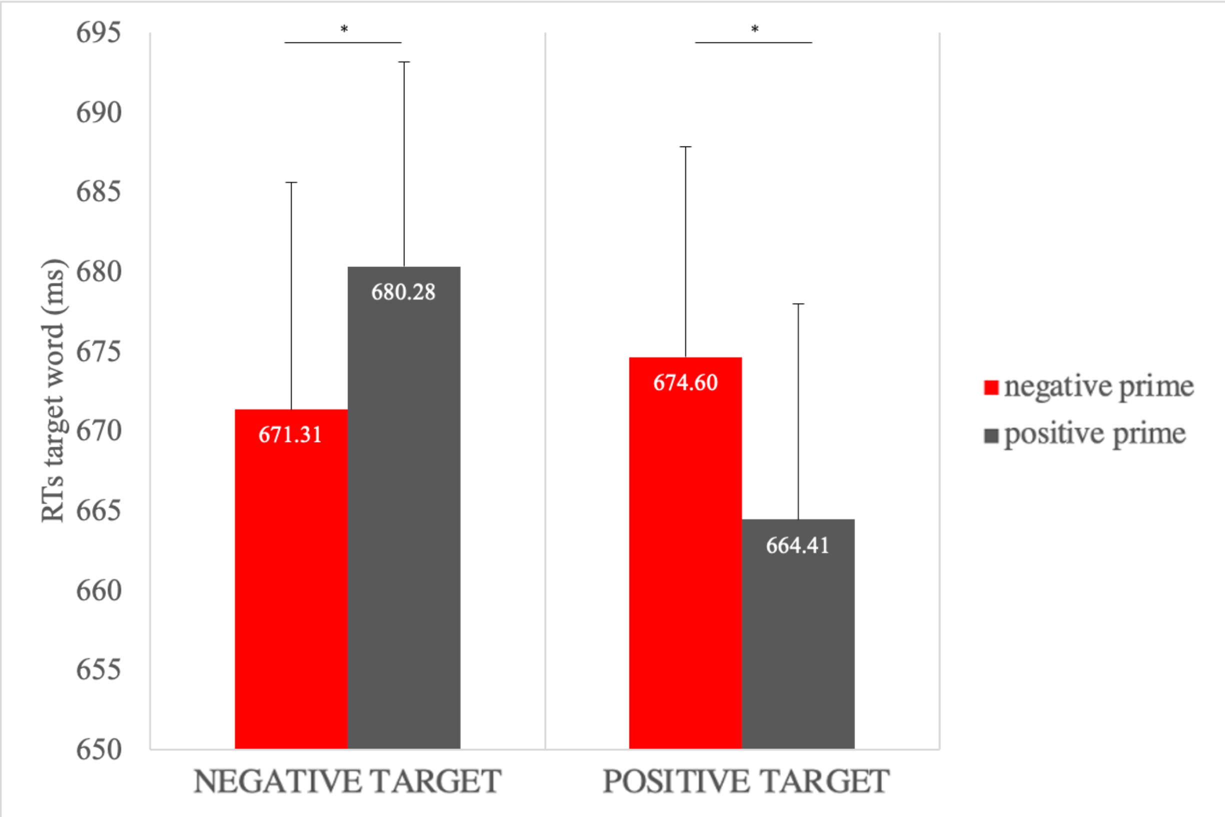
The same statistical analyses were conducted as in Experiment 1 by removing the gender of the participants as a factor, since the task was administered only to female participants.

2.3.2. Results

In total, 10.34% of the trials were excluded from the analyses because the RTs exceeded ± 2 SD. For accuracy scores in the 2 × 2 ANOVA, the main effect of target valence was significant [F (1, 29) = 4.559, p = .041, η_p^2 = .136], so that responses to the negative target were more accurate than to the positive target. In addition, a marginally significant priming effect was represented by prime valence x target valence interaction [F (1, 29) = 4.100, p = .052, η_p^2 = .124] supporting the initial hypothesis. To further examine this interaction, we conducted paired-sample t-tests which, however, detected no significant effect.

The analysis of RTs showed a significant effect of the prime valence x target valence interaction [F (1, 29) = 7.439, p = .011, η_p^2 = .204]. To further investigate the interaction, paired-sample t-tests showed significantly faster RTs in both affective congruent and incongruent conditions, confirming our hypotheses. Specifically, the positive target was processed faster when preceded by a positive prime [t (29) = -2.344, p = .013, Cohen's d = -.428]; similarly, the negative target was processed faster when preceded by a negative prime [t (29) = -2.344, p = .015, Cohen's d = -.419] (see Figure 3).

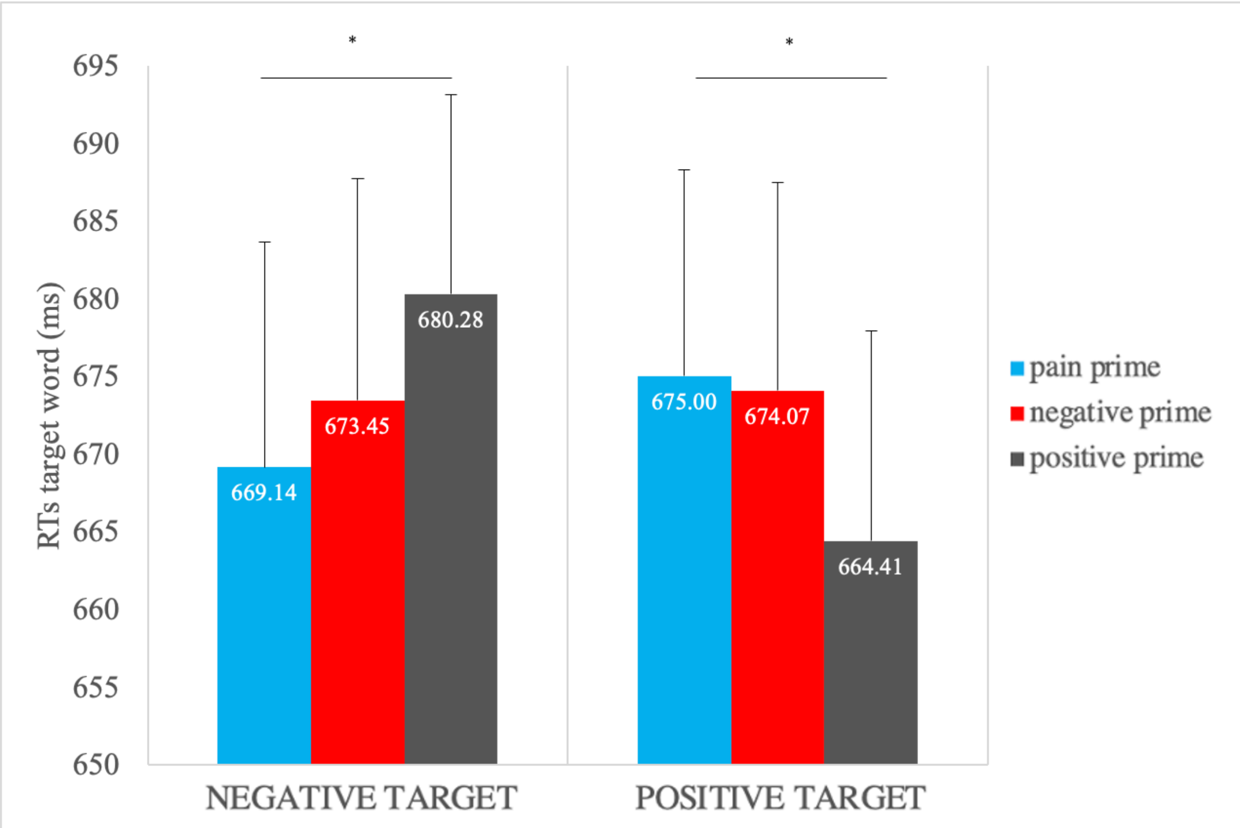
Figure 3. Affective priming effect for the "valence" factor (significant comparisons showing the priming effect for the positive and negative targets are indicated with an asterisk).



A second analysis of variance was then performed separating negative primes and pain primes. The 3 × 2 ANOVA on the accuracy scores showed a significant main effect of target valence [F (2, 29) = 5.828, p = .022, η_p^2 = .167] so that responses to the negative target were more accurate than to the positive targe. On the other hand, the main effect of prime valence appears to be marginally significant so that responses to positive primes were more accurate than to negative and pain primes [F (2, 29) = 2.660, p = .079, η_p^2 = .084]. The data also showed a significant priming effect represented by the prime valence x target valence interaction [F (2, 58) = 7.392, p = .001, η_p^2 = .203]. To examine the source of this interaction paired samples t-tests were conducted, which however detected no significant effect.

The analysis of RTs showed a significant priming effect, as indicated by prime valence x target valence interaction [F (1.8, 51.2) = 5.129, p = .012, η_p^2 = .150]. Paired- sample t-tests showed significantly faster RTs when the positive target was preceded by positive prime rather than pain prime [t (29) = -1.902, p = .034, Cohen's d = -.347] and a significantly faster RTs when the negative target was preceded by pain prime [t (29) = -2.572, p = .008, Cohen's d = -.470] and not by negative one (see Figure 4).

Figure 4. Priming effect for the semantic factor (significant comparisons highlighting the priming effect for the positive and negative target are indicated with an asterisk).



Correlations analyses between the subscales of the questionnaires and the differences in accuracy scores showed that the accuracy scores of the negative priming condition (difference in scores between the pain prime-negative target and prime positive - negative target) correlated negatively with the *Drive* subscale of the BIS/BAS questionnaire [Spear- man's rho = -.476, p = .008]. As for RTs, no significant correlation was found between the scores of each of the subscale of the questionnaires and the congruent and incongruent conditions.

2.3.3. Discussion Experiment 2

In Experiment 2, we used the same affective priming paradigm as in Experiment 1 on a sample of female participants, modifying the SOA parameter. Experiment 2 demonstrated an affective priming effect between the affective congruent and incongruent conditions, where the participant was facilitated to respond faster and more accurately to the target when it was preceded by a prime of the same valence. Specifically, an affective priming effect emerged for positive stimuli, confirming the effect previously described in the literature (Aguado et al., 2013; Contreras-Huerta et al., 2013;

Gibbons et al., 2014). Meanwhile, the affective priming for negative congruent conditions supported the hypothesis according to which a negative prime may facilitate the response to a negative target (Meagher et al., 2001). Interestingly, a subsequent analysis, considering the negative prime and pain prime separately, revealed that the affective priming effect described above only emerged when the negative target was preceded by a pain prime, but not by a negative prime. Therefore, the semantics of pain embodied in the prime appeared to have facilitated the processing of the negative target.

Our study seems to shed light on the mechanism by which valence and semantics interact using words by generating a specific response to pain. In the literature, it has been widely discussed how the valence of a stimulus interacts with its semantics generating a specific response for each emotion (Fazio et al., 1986). Unfortunately, there is still no agreement on the nature and direction of this interaction regarding negative stimuli, or pain. The most accepted theory is the one proposed by Yamada and Decety (2009), who hypothesized that the evaluation of a pain stimulus is facilitated by the implicit processing of information associated with pain. However, we are not aware of any studies that have used word stimuli associated with pain to study how their implicit processing might influence the subsequent evaluation of a negative stimulus.

Experiment 2 was crucial in detecting a priming effect even for negative stimuli. The facilitation effect generated by pain primes on negative targets suggests that the effect was specific to pain content to the extent that the negative priming effect shown in the first analysis may have been entirely generated by the same negative primes associated with pain. The negative correlation of the accuracy scores in the negative priming condition with the *Drive* subscale of the BAS scale (Leone et al., 2002) strengthens our results: high scores on this subscale indicate a strong tendency to pursue appetitive goals and to detect reward signals in the environment. Thus, a pain prime might promote the processing of negative information, potentially inhibiting the activation of approach behaviors. A possible parameter that may have contributed to the emergence of this effect is the modification is the stimulus onset asynchrony (SOA), which is the interval between the prime and the target onset. Previous research has amply demonstrated how the affective priming effect is sensitive to this parameter (Fazio et al., 1986; Klauer & Musch, 2003).

First, these results suggest that the affective congruence effect may lie in the affective and semantic characteristics of a stimulus itself on the allocation of attentional resources. In fact, as already discussed by Klauer (1997), individuals automatically process the information embedded in the negative prime in order to allocate more attentional resources for responding to negative threats. In this way, they become quickly aware of dangers in the environment and can react with faster responses to preserve their survival (Klauer, 1997). The same mechanism is echoed by the motivational priming theory (Davidson & Irwin, 1999; LeDoux, 2000), according to which the pain prime pre-activates the aversive system to respond to the arrival of a subsequent negative information and facilitates the individual to generate avoidance responses as quickly as possible (Davidson & Irwin, 1999; LeDoux, 2000).

However, it is still not clear how the specific semantic content of an emotion, such as pain, can generate specific affective priming effect. It remains a hypothesis that, in accordance with the spreading activation theory, the negative valence of the prime pre-activates the network of concepts associated with the prime, facilitating the subsequent processing of a target of the same valence (Fazio et al., 1986; Murphy & Zajonc, 1993). This effect is then amplified by the semantics of pain contained in the prime. Indeed, pain has properties that are peculiar to other emotional categories because of its relevance in terms of the survival of the species. It is therefore reasonable to assume that it plays a key role in guiding the processing of negative stimuli and promoting avoidance behaviors from possible threats to preserve the individual (Fazio et al., 1986; Gibbons et al., 2018).

According to Aguado et al. (2018) in literature, the heterogeneity of results on affective priming on negative stimuli can be attributed to the fact that negative stimuli are represented by diverse emotional categories (e.g., anger, fear, pain) that elicit specific effects. A study by Rossell and Nobre (2004) showed that word pairs belonging to the category of fear generate modest priming effect compared to words belonging to the sadness category which, in contrast, produces an inhibitory effect on the elaboration of negative targets. It follows that affective categories within the negative valence should be considered separately, which is why many studies failed to detect an affective priming effect for negative stimuli (Rossell & Nobre, 2004).

In this regard, another parameter that may have contributed to the heterogeneous results in the literature is the semantic relationship between prime and target, which is not often included as a variable in affective priming studies (Hu & Liu, 2019). In their study, Hu and Liu (2019)showed that when the semantic relationship between prime and target was strong, a significant priming was detected. In contrast, when the relationship between the two was weak, no effect was observed. Considering future experiments, it is appropriate to control for this variable (e.g., Hu & Liu, 2019); Rossell & Nobre, 2004).

One limitation of our experiment was that the sample population consisted solely of females. Previous research showed that there might be gender differences in response to this particular paradigm, with females exhibiting stronger effects than male (Hermans et al., 1998; Schirmer et al., 2005). Moreover, studies on pain processing have extensively covered gender differences (Rhudy & Williams, 2005). It has been found that females tend to experience more intense reactions to pain stimuli, and have a different perception of risk compared to males (Charness & Gneezy, 2012). Based on these differences and our previous study using the same paradigm (Gilioli, Borelli, & Pesciarelli, 2023), we initially chose to focus on a female sample in order to potentially maximize the effect. However, to ensure the generalizability of our results, it is necessary to also extend the study to male participants.

A second limitation of our study was the lack of a measure confirming that negative words not associated with pain were not actually perceived as painful. Such a measure can be obtained through a normative pre-test or by assessing the semantic closeness to the word "pain." In future research, it will be beneficial to define the semantic relationship of stimuli in a more objective manner.

In conclusion, it is possible that the dual nature of pain itself may have led to conflicting results in the literature. However, our studies gain insight into the mechanism by which pain is automatically processed to the extent that it facilitates the subsequent processing of negative information. To the best of our knowledge, Experiment 2 represents the first study to have identified affective priming with word stimuli associated with pain. This supports the idea that the cognitive system deals with the affective and semantic valence of a stimulus, considering how they interact with each other in the stimulus evaluation. Future research will benefit from investigating the time course of the elaboration of these two stimulus properties.

Chapter 3

Electrophysiological correlates of semantic pain processing in the affective priming

3.1. Introduction

Our behavioral studies on affective priming (Chapter 2- Study 1) demonstrated how the cognitive system automatically evaluates the affective content of an emotional stimulus in terms of positive and negative valence. Likewise, its embedded semantic content plays a part in generating specific responses to each emotion, particularly in our case, to pain. Several studies have shown that the affective and semantic valence are processed at two different stages of stimulus evaluation but the neural dynamics of these processes remain elusive (Aguado et al., 2018; Comesaña et al., 2013; Diéguez-Risco et al., 2015; Eder et al., 2012; Hartigan & Richards, 2016; Herring et al., 2011; Hietanen & Astikainen, 2013; Song et al., 2019). For this reason, it is interesting to study the time course of the elaboration of affective and semantic valence.

Event-related potentials (ERPs) indeed represent an online measure of such an effect with a temporal resolution within millisecond range. In literature, several studies on affective priming showed that the incongruency of valence between two stimuli can be indexed by ERPs components as the N400 (Eder et al., 2012; Hietanen & Astikainen, 2013; Steinbeis & Koelsch, 2011; Zhang et al., 2006, 2010), which is a negative-ongoing wave peaking around 400 ms after stimulus onset typically associated with the violation of semantic content (Kutas & Hillyard, 1984). Despite most of the studies found this effect, some reported a null effect (Herring et al., 2011), or even a reverse priming effect with a greater amplitude of the N400 in affective congruent conditions (Aguado et al., 2013; Paulmann & Pell, 2010; Wang & Zhang, 2016). In addition, another ERP component often modulated by the affective incongruency is the LPP can appear in a window between 400-700 ms after stimulus onset and is sensitive to the evaluation of properties of stimuli and to the inconsistency of valence (Aguado et al., 2013; Comesaña et al., 2013; Hartigan & Richards, 2016; Herring et al., 2011; Hietanen & Astikainen, 2013). As for the N400, results are still inconsistent with some studies reporting no effect (C. Wu et al., 2021) or even a reverse priming effect (Eder et al., 2012; Hartigan & Richards, 2016) due to several overlapping components that appear in that time window. In particular, few studies pointed out how an earlier phase of the LPP (400-600 ms) may indicate the automatic allocation of attention to salient stimuli, while a later phase (post 600 ms) is affected by the top-down influence explicitly interpret the stimulus (Olofsson et al., 2008) or by contextual factors

(Foti & Hajcak, 2008). The inconsistency of these results may lie in the fact that the negative valence is generally treated as a single semantic domain when, on the contrary, it embraces a heterogenous group of semantic categories (Rossell & Nobre, 2004). For this reason, it is possible to speculate that when the cognitive system needs to determine the priority of a stimulus, the negative valence of the stimuli interacts with their semantic content generating specific responses for each type of emotion (Fazio et al., 1986). Thus, pain may represent an appropriate model to understand if the specificity of the semantic content of a stimulus present in the environment can interact with the valence to the point of influencing the subsequent elaboration of positive and negative information.

In light of this, the present research aimed at investigating the time course of the implicit processing of pain words, analyzing the ERPs correlates of this effect. For this purpose, we replicated our previous behavioral experiments (Chapter 2- Study 1) using the EEG technique. In Chapter 2, we adopted an affective priming paradigm and presented healthy participants with prime words with positive and negative valence (associated and not-associated with pain) and target words with positive and negative valence (not-associated with pain). Participants had to evaluate the valence of the target (valence judgment task) by pressing one of two buttons.

In the present study, our first goal was to confirm the behavioral findings of our prior work. We recruited a different sample of participants and asked them to perform the same task on the same stimuli while recording their electrophysiological activity as well as their reaction times (RTs). Our second goal was to study the electrophysiological correlates of this effect by focusing on two main ERPs components, the N400 and LPP. To the best of our knowledge, this is the first study to apply ERP component analysis to an affective priming paradigm involving word stimuli associated with pain. We hypothesized that if pain-related semantics elicit a distinct response, then these components would capture it to a greater extent at an electrophysiological level. However, due to the limited and inconclusive nature of previous research, it remains unclear whether this effect is present and in what direction. Therefore, it is reasonable to consider the possibility that the priming effect may also occur in other ERP time windows.

3.2. Methods

3.2.1. Participants

Thirty-seven students at the University of Modena and Reggio Emilia, all females (age range: 19- 51 yrs; mean age=25.16; SD = 7.49) participated in the experiment for course credit. All participants were right-handed (L.Q.= 91.7) as assessed by the Italian version of the Edinburgh

Handedness Inventory (Oldfield, 1971), and they had normal or corrected-to-normal visual acuity, no history of neurological or mental disorders, and they were Italian native speakers.

Three participants were excluded from the analyses: the first due to a recording error of the experimenter, the second started to perform the task before the recording was initiated, and the last needed to be excluded since the experiment was interrupted by an external issue. Therefore, the statistical analyses were performed on 34 female subjects (age range:19-51 yrs; mean age=24.65; SD = 7.21). The sample size was established based on heuristic evaluations of the literature on affective priming and our previous research (Chapter 2), which reports numerous studies with samples of 22-33 subjects (C. Wu et al., 2021; Yamada & Decety, 2009). We also conducted a posteriori sensitivity power analysis (Lakens, 2022) using G*Power 3.1. (Faul et al., 2007) according to which given N=34, $\alpha = .05$ and a power = 80% a minimum partial equal to $\eta^2 = .1968$ was found, consistent with the literature on this topic.

The choice of selecting an entire sample of female participants was based on Experiment 1 and 2.

3.2.2. Stimuli

The stimuli and experimental conditions are the same as those presented for Experiment 1 and 2. Each prime-target pair was also controlled for semantic relatedness which was calculated using the *Wup* similarity measure (Wu & Palmer, 1994) in WordNet::Similarity library software (Pedersen et al., 2004). WordNet groups words into sets of synonyms called synsets and describes semantic relationships between them. The *Wup* measure calculates the similarity based on the shortest distance between two words in the WordNet hierarchy and their position relative to their least ancestor. The score can range between 0 and 1, where 1 represents the closest semantic relatedness.

3.2.3. Procedure

The procedure is the same as that used in Experiment 2, with the only difference in the prime duration set at 150 ms. The set up lasted approximately 30 minutes and the experiment lasted approximately 35 minutes. The total experiment had a total duration of 65 minutes.

3.2.4. Questionnaires

The questionnaires administered to the participants are the same of those used in Experiment 1.

3.2.5. EEG recording and analysis

The EEG data was recorded continuously via 64 active electrodes (ActiCap Slim, BrainProducts) placed on the scalp according to the International 10–10. Electrical activity was amplified and sampled at 1000 Hz by a 24-bit ActiCHamp Plus System (BrainProducts) and recorded with BrainVision recorder software (BrainProducts, version 1.25.0101) running on a Windows 10 computer. All electrodes were recorded with the online reference located at FCz. Two electrodes were placed over the left and right mastoids to serve as an offline reference, two were placed at the external ocular canthi of both eyes to monitor horizontal eye movements (HEOG) and one was placed under the left eye to monitor blinks (VEOG). Electrical impedances were kept below 20 kΩ.

Brain Vision Analyzer 2 (Brain Products, Gilching, Germany) was used to perform off-line signal processing analyses. The EEG signal was bandpass filtered between 0.1 and 80 Hz and referenced offline to the average activity of the two mastoids. Artifact activity was rejected using a semiautomated procedure, with artifacts identified by the following criteria: Gradient, with 75 µV maximal allowed voltage step; Max–Min with 200 ms maximal allowed absolute difference; Low activity, with 0.5 µV/100 ms lowest allowed activity. Data with excessive blinks were adaptively corrected using ICA. 1000-ms epochs containing the ERP elicited by the target word were extracted. A 200 ms pre-stimulus baseline was used in all analyses. Segments including artifacts due to activity exceeding ± 100 µV in amplitude were rejected.

The data has been filtered at 30Hz with the sole purpose of better graphic visualization. The statistical analyses were conducted on the data initially filtered at 0.1-80 Hz. Based on visual inspection of grand average ERP waveforms and in line with previous literature, the following components were identified for target onset at frontal (F3, Fz, F4), central (C3, Cz, C4), and parietal (P3, Pz, P4) scalp sites: N400 from 300 to 500 ms after target onset; LPP from 500 to 700 ms after target onset. For each ERP component amplitude was measured as mean activity within the respective time window.

3.2.6. Statistical analyses

Statistical analyses for the behavioral scores (i.e., accuracy scores and RTs) are the same of Experiment 2. In addition, to control for potential confounding effects of primes and targets familiarity, length in letters, valence, arousal, and semantic relatedness we added them as covariates in four analyses of covariance on RTs and accuracy scores, one with prime valence as a factor and the other with prime semantics as a factor.

Then, ERPs analyses were performed on the EEG activity. At the ERP level, ERP effects time-locked to the onset of the target were evaluated considering 6 clusters of electrodes representing the mean amplitude of three electrodes in close position: Anterior (F3, Fz, F4), Central (C3, Cz, C4), Posterior (P3, Pz, P4), Left (F3, C3, P3), Midline (Fz, Cz, Pz), Right (F4, C4, P4).

A repeated-measures 2x2x3x3 ANOVA was conducted on mean ERP amplitudes with prime valence (positive, negative), target valence (positive, negative), longitude (anterior, central, posterior), and latitude (left, midline, right) as within-subject factors. Secondly, to consider the effect of the semantic content associated to the negative prime, a repeated-measures 3x2x3x3 ANOVA was performed on ERP amplitudes with prime semantics (positive, negative, pain), target valence (positive, negative), longitude (anterior, central, posterior), and latitude (left, midline, right) as within-subject factors. To further understand the nature of the interactions, both analyses were followed by separate ANOVAs which were run on the positive and negative target valence. Additionally, post-hoc mean comparisons were employed to further examine significant interactions.

In addition, we analyzed the influence of individual differences in pain processing measured by the above-mentioned questionnaires on the behavioral and ERP effects. For each subscale of the questionnaires, the correlation with accuracy scores and RTs Δ congruent-incongruent conditions was measured by the Spearman coefficient for non-parametric measures. As well the correlation with ERP amplitudes of all electrodes Δ congruent-incongruent conditions was measured by the Spearman coefficient for non-parametric measures. This was calculated for both time windows (300-500 and 500-700 ms).

To account for violations of sphericity, the Greenhouse–Geisser procedure was used to correct degrees of freedom: only corrected significance levels are reported. The level of significance for all statistical analyses was set to $p<0.05$. Holm correction was applied for multiple comparisons and only corrected p-values are reported. The main effects of prime valence and target valence in the omnibus ANOVAs were not central to the questions under study. Therefore, they are reported but not discussed. Here, we discussed only the interaction between prime valence and target valence which was of interest to the study. In the separate ANOVAs for the target valence, the main effect of the prime valence was crucial to the analyses: for this reason, it has been discussed.

3.3. Results

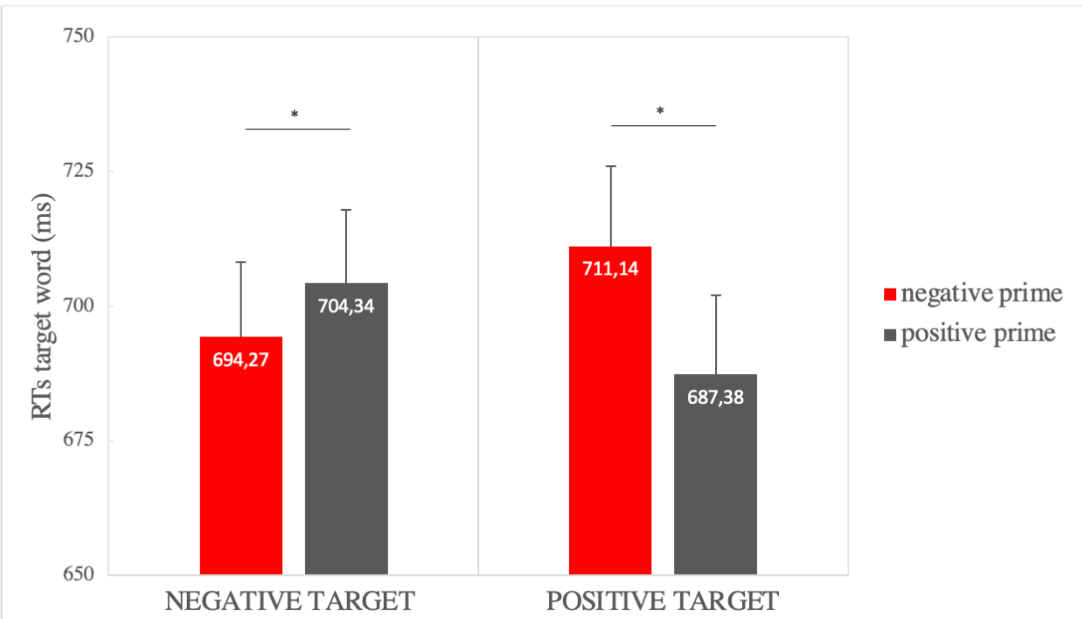
3.3.1. Behavioral results

Results from the two ANCOVAs on stimuli accuracy did not reveal any confounding effect of prime and target familiarity, length, valence, arousal, semantic relatedness neither with prime valence nor with prime semantics as a factor. Results from the two ANCOVAs on stimuli RTs revealed a possible confounding effect of target length ($p < .001$) when prime valence was a factor and a possible confounding effect of target length ($p < .001$), and target arousal ($p = .008$) when prime semantics was a factor. Because the overall results with and without these potentially confounding variables were the same, they have not been included in the analyses on participants' RTs and accuracy and will not be further discussed.

Overall, 6.6% of trials were excluded from the analyses because the RTs exceeded ± 2 SD. In order to investigate the role of the prime valence, we performed repeated-measures 2x2 ANOVAs on the accuracy scores and the mean RTs. The analysis on the accuracy scores showed a significant main effect of target valence [$F(1,33) = 6.13$, $p= .019$, $\eta_p^2 =.16$] so that responses to the negative target ($\mu = 0.96$, SE= 0.001) were more accurate than to the positive one ($\mu = 0.94$, SE= 0.009).

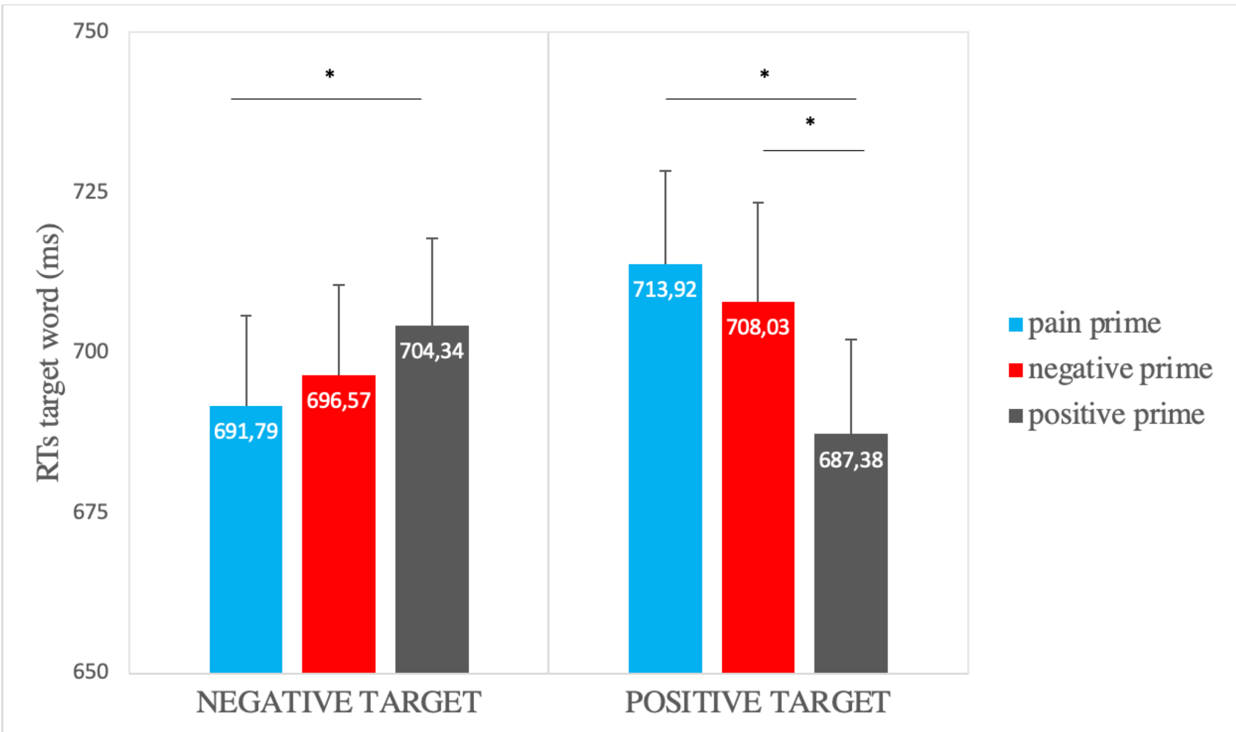
The analysis on RTs showed a significant main effect of prime valence [$F(1,33) = 8.56$, $p= .006$, $\eta_p^2 = .21$] so that the positive prime ($\mu = 695.86$, SE= 8.48) was elaborated faster than the negative one ($\mu = 702.71$, SE= 8.43), and a significant prime valence x target valence interaction [$F(1,33) = 12.289$, $p= .001$, $\eta_p^2 = .271$]. Paired sample t-tests showed significantly faster RTs when the positive target was preceded by a positive prime ($\mu = 687.38$, SE= 14.74) rather than a negative prime ($\mu = 711.14$, SE= 14.85) [$t (33) = -4.4$, $p= 0.002$ $p = <.001$, Cohen's d= -.75]; and significant faster RTs when the negative target ($\mu = 694.27$, SE= 13.94) was preceded by a negative prime rather than a positive one ($\mu = 704.34$, SE= 13.57) [$t (33) = -1.89$, $p = .034$, Cohen's d= -.32], as shown in Figure 2.

Figure 2. Affective priming effect on RTs for the "valence" factor (in the graph significant comparisons are indicated with *: this highlights the priming effect for positive and negative targets). Error bars represent standard errors of the mean.



To investigate the role of the prime semantics, we performed repeated measures 3x2 ANOVAs on the accuracy scores and the mean RTs. The analysis on accuracy scores showed a significant main effect of target valence [$F(1,33) = 5.58$, $p= .024$, $\eta_p^2 = .15$] so that responses to the negative target ($\mu= 0.96$, SE= 0.001) were more accurate than to the positive one ($\mu= 0.94$, SE= 0.007). The analysis on RTs showed a significant main effect of prime semantics [$F(1.8, 60.9) = 3.15$, $p= .05$, $\eta_p^2 = .09$] so that the positive prime ($\mu= 695.86$, SE= 8,48) was elaborated faster than the negative ($\mu= 702.3$, SE= 5.73) and the pain one ($\mu= 702.86$, SE= 11.06); and a significant prime semantics x target valence interaction [$F(1.5, 49.85) = 10.35$, $p= < .001$, $\eta_p^2 = .24$]. Paired samples t-tests showed significantly faster RTs when the positive target was preceded by a positive prime ($\mu= 687.38$, SE= 14.74) rather than a pain prime ($\mu= 713.92$, SE= 14.49) [$t (33) = -4.4$, $p = .003$, Cohen's d= -.75] or a negative prime ($\mu= 708.03$, SE= 15.50) [$t (33) = -3.59$, $p = .003$, Cohen's d= -.62] and significantly faster RTs when the negative target was preceded by a pain prime ($\mu= 691.79$, SE= 14.07) rather than a positive one ($\mu= 704.34$, SE= 13.57) [$t (33) = -2.21$, $p = .017$, Cohen's d= -.38] (see Figure 3).

Figure 3. Affective priming effect on RTs for the "semantic" factor (in the graph significant comparisons are indicated with *: this highlights the priming effect for positive and negative targets). Error bars represent standard errors of the mean.



3.3.2. ERP results

Grand-averaged ERPs elicited by the different experimental conditions are represented in Figure 4 and their topographical maps in Figure 5.

Figure 4. Grand-averaged ERP waveforms elicited by positive and negative target words for the valence manipulation condition (*a* and *c* panels) and the semantic manipulation condition (*b* and *d* panels) as a function of prime type.

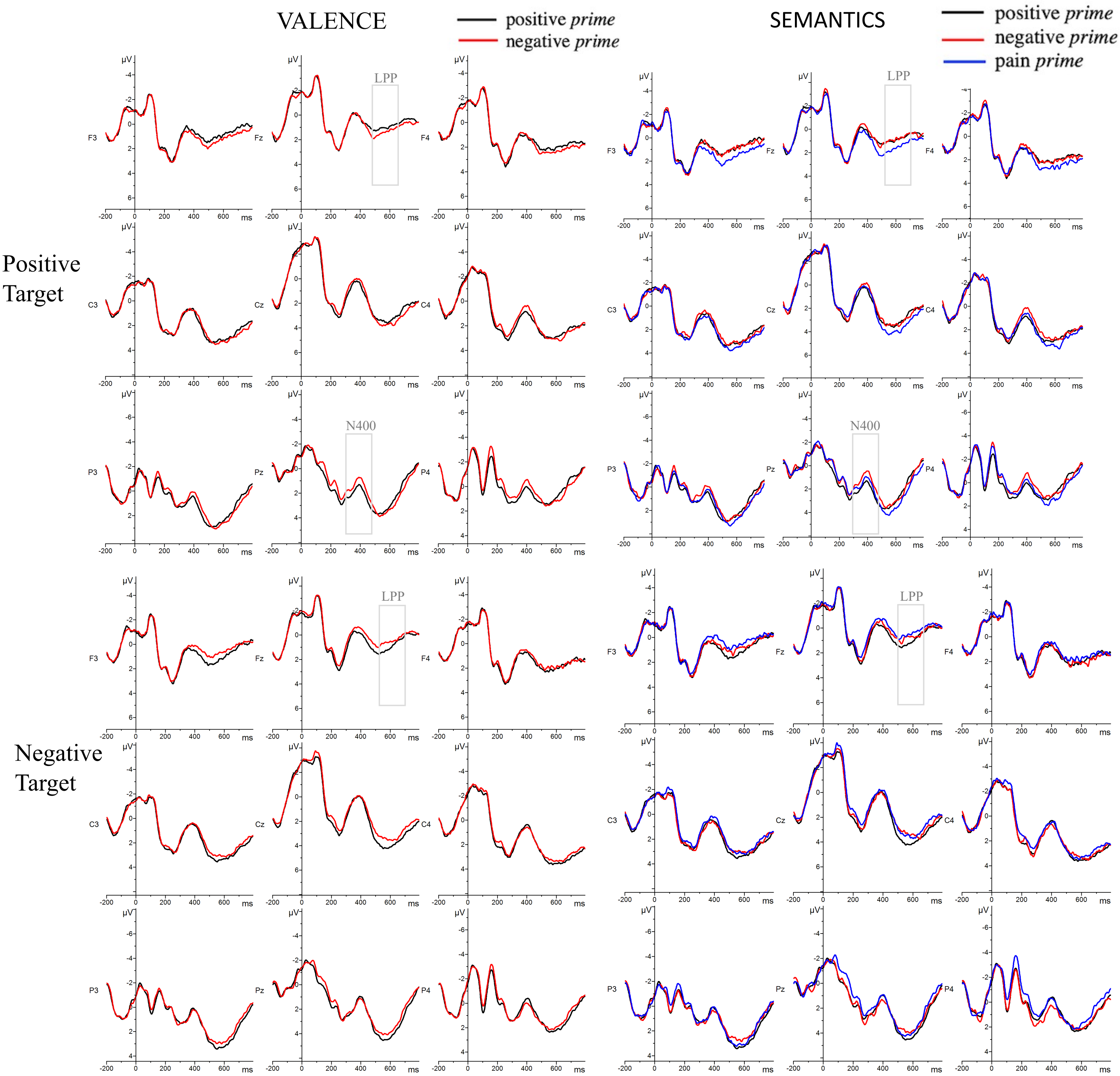
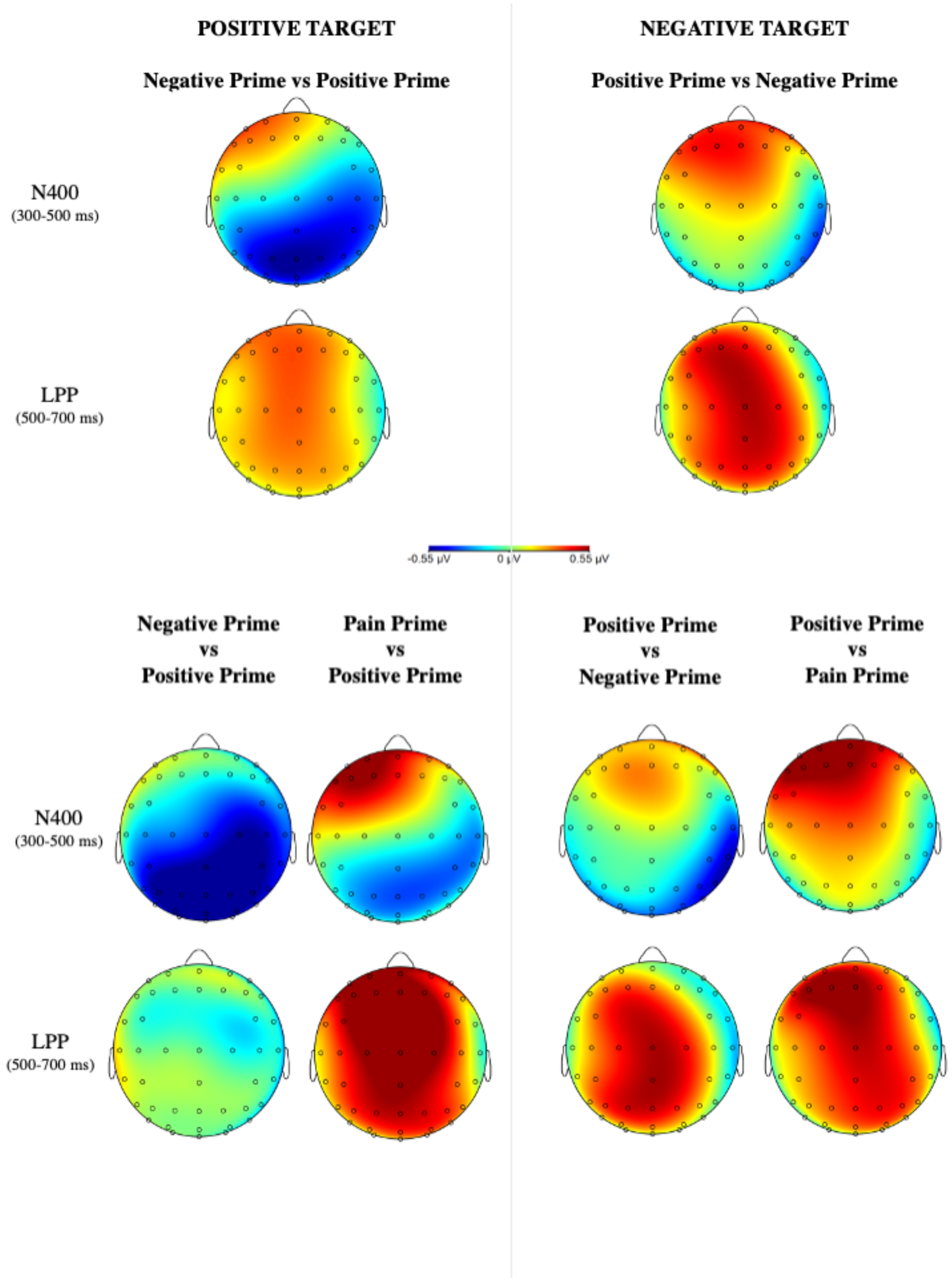


Figure 5. Topographical scalp distribution for positive and negative targets for the valence manipulation conditions (a panel) and for the semantic manipulation condition (b panel) in the two critical time windows, created by subtracting incongruent conditions and congruent conditions.



3.3.2.1. N400

To investigate the role of prime valence, we performed repeated-measures 2x2x3x3 ANOVAs on ERPs amplitudes which showed a marginally significant main effect of prime valence [$F(1,33)= 3.63$; $p = .066$; $\eta_p^2 = .1$] so that the negative prime elicited larger negative waveforms (µV=1.05, SE=0.32) rather than the positive one (µV=1.21, SE=0.32). The analysis also showed the following significant interactions: target valence x longitude [$F(1.41, 46.66)= 7.22$; $p = .005$; $\eta p^2 = .18$]; latitude x prime valence x target valence [$F(1.82, 60.16)= 4.32$; $p = .02$; $\eta_p^2 = .12$]; longitude x prime valence x target valence [$F(1.33, 43.8)= 11.99$; $p = <.001$; $\eta_p^2 = .27$]. To further explore these interactions, the ERPs amplitudes of positive target and negative target were analyzed separately. The 2x3x3 ANOVA on the positive targets showed a significant longitude x prime valence interaction [$F(1.28, 42.34)= 10.37$; $p = .001$; $\eta_p^2 = .24$]. Post-hoc analyses revealed a larger negative waveform when the positive target is preceded by a negative prime (µV=0.99, SE=0.43) rather than a positive prime (µV=1.46, SE=0.43) at posterior positions.

As for the negative target, the 2x3x3 ANOVA on the negative targets showed the subsequent significant interactions: latitude x prime valence [$F(1.87, 61.65)= 6.02$; $p = .005$; $\eta_p^2 = .15$]; longitude x prime valence [$F(1.41, 46.59)= 4.09$; $p = .036$; $\eta_p^2 = .11$]. No effects in the post-hoc analyses resulted significant.

To investigate the role of the prime semantics, a further 3x2x3x3 ANOVA showed the following significant interactions: prime semantics x target valence [$F(1.67, 55.06)= 5.38$; $p = .011$; $\eta_p^2 = .14$], longitude x target valence [$F(1.45, 47.81)= 13.86$; $p =<.001$; $\eta p^2 = .3$], longitude x prime semantics x target valence [$F(2.5, 82.6)= 4.52$; $p = .009$; $\eta_p^2 = .12$]; and a marginally significant latitude x longitude x prime semantics x target valence [$F(4.7, 155.45)= 2.1$; $p = .074$; $\eta_p^2 = .06$]. To further explore these interactions, the ERPs amplitudes of positive and negative targets were analyzed separately. The 3x3x3 ANOVA on the positive targets showed a significant main effect of prime semantics [$F(1.92, 63.35)= 5.48$; $p = .007$; $\eta_p^2 = .14$] so that the positive target elicited larger negative waveforms when preceded by a negative prime (µV=0.91, SE=0.35) rather than a pain one (µV=1.31, SE=0.35), and when it was preceded by a negative prime rather than a positive one (µV=1.29, SE=0.35). The analysis also showed a significant longitude x prime semantics interaction [$F(2.44, 80.64)= 3.71$; $p = .021$; $\eta_p^2 = .1$]. Post-hoc analyses revealed a larger negative waveform when the positive target is preceded by a negative prime (µV=0.8, SE=0.43) rather than a positive one (µV=1.46, SE=0.43) at posterior positions.

The 3x3x3 ANOVA on the negative targets showed a marginally significant latitude x longitude x prime semantics interaction [$F(5.62,185.55)= 2.17$; $p = .052$; $\eta_p^2 = .06$]. No significant post-hoc analyses resulted significant.

3.3.2.2. LPP

To investigate the role of prime valence, we performed repeated-measures 2x2x3x3 ANOVA on ERPs amplitudes which showed the following significant interactions: prime valence x target valence [$F(1, 33) = 7.38$; $p = .010$; $\eta_p^2 = .18$], longitude x target valence [$F(1.44, 47.54) = 11.95$; $p = <.010$; $\eta p^2 = 0.27$], and a marginally significant latitude x prime valence x target valence interaction [$F(1.7, 56.08) = 3.20$; $p = .056$; $\eta_p^2 = .09$]. To further explore these interactions, the ERPs amplitudes of positive target and negative target were analyzed separately. The 2x3x3 ANOVA on the positive targets showed a significant main effect of the prime valence [$F(1, 33) = 4.21$; $p = .048$; $\eta_p^2 = .11$] in which the positive target elicited larger positive waveforms when preceded by a negative prime (μV=2.33, SE=0.46) rather than a positive prime (μV=2.07, SE=0.46). The 2x3x3 ANOVA on the negative targets showed a significant main effect of prime valence [$F(1, 33) = 6.13$; $p = .019$; $\eta_p^2 = .16$] in which the negative target elicited larger positive waveforms when preceded by a positive prime (μV=2.58, SE=0.41) rather than a negative one (μV=2.23, SE=0.41). In addition, the analysis also showed a significant latitude x prime valence interaction [$F(1.82, 60.11) = 4.83$; $p = .014$; $\eta_p^2 = .13$]. Post-hoc analyses revealed larger positive waveforms when the negative target is preceded by a positive prime (μV=2.92, SE=0.43) rather than a negative (μV=2.44, SE=0.43) one at midline positions.

Thereafter, to investigate the role of the prime semantics, a further 3x2x3x3 ANOVA was performed which showed the following significant interactions: prime semantics x target valence [$F(1.83, 60.22) = 8.40$; $p = <.001$; $\eta_p^2 = .2$], longitude x target valence [$F(1.44, 47.44) = 11.44$; $p = < .001$; $\eta p^2 = .26$], and a marginally significant latitude x longitude x prime semantics x target valence interaction [$F(4.78, 157.45) = 2.21$; $p = .059$; $\eta_p^2 = .06$]. To further explore these interactions, the ERPs amplitudes of positive target and negative target were analyzed separately. The 2x3x3 ANOVA on the positive targets showed a significant main effect of prime valence [$F(1.95, 64.45) = 8.99$; $p = < .001$; $\eta_p^2 = .21$] with larger positive waveforms when preceded by a pain prime (μV=2.6, SE=0.46) rather than a negative one (μV=2.06, SE=0.46) and a positive one (μV=2.06, SE=0.46). The 2x3x3 ANOVA on the negative targets showed a marginally significant main effect of prime semantics [$F(1.98, 65.48) = 3.08$; $p = .053$; $\eta_p^2 = .085$] so that the negative target elicited larger positive waveforms when preceded by a positive prime (μV=258, SE=0.41) rather than a pain prime (μV=2.18, SE=0.41). Moreover, the analysis also showed a significant latitude x prime semantics interaction [$F(3.59, 118.41) = 2.83$; $p = .032$; $\eta_p^2 = .08$] and only a marginally significant latitude x longitude x prime semantics interaction [$F(5.17, 170.69) = 2.00$; $p = .079$; $\eta p^2 = .06$]. No effects in the post-hoc analyses resulted significant.

3.3.3. Correlations

To test the influence of individual differences in pain processing on the accuracy and RT effects, we performed the correlation between the scores in the questionnaires' subscales and the behavioral effects both for prime valence and prime semantics. In the analysis on prime valence, the correlation between the questionnaire's subscales and the difference in accuracy scores Δ between congruent and -incongruent conditions showed that both the priming effects associated with the negative target and the positive target were positively correlated to the subscale Magnification of the PCS questionnaire (respectively Spearman's rho = .42, p = .001; Spearman's rho = .35, p = .042).

In the analysis on prime semantics, the correlation analysis on accuracy scores showed a negative correlation between the priming effect associated with the negative target (pain prime-negative target vs positive prime-negative target) and the subscales of the Empathic Concern (Spearman's rho = -.33, p = .027) and the Perspective Taking (Spearman's rho = -.37, p = .031) of the IRI questionnaire. An additional negative correlation was detected between the priming effect associated with the negative target (negative prime-negative target vs positive prime-negative target) and the Magnification subscales of the PCS questionnaire (Spearman's rho = -.38, p = .029). The correlational analyses on RTs did not show any significant results.

In addition, we analyzed the individual differences in pain processing on the ERP effect. In the analysis on prime valence for both the ERP components, the correlation analysis between questionnaires' subscales and the difference in mean amplitudes for all electrode sites Δ between congruent and -incongruent conditions did not show any significant results. In the analysis on the prime semantics, the correlation analyses on N400 mean amplitudes showed that the priming effects associated with the positive target (positive prime-positive target vs negative prime-positive target) correlated with both the BIS scale (Spearman's rho = .43, p = .012), the Personal Distress subscale of the IRI questionnaire (Spearman's rho = .40, p = .019), and the Rumination subscale of the PCS questionnaire (Spearman's rho = .354, p = .04). The correlation analyses on LPP mean amplitudes showed that the priming effects associated with the negative target (pain prime-negative target vs negative prime-negative target) correlated with both the Fantasy subscale of the IRI questionnaire (Spearman's rho = .35, p = .04), and the Rumination subscale of the PCS questionnaire (Spearman's rho = .38, p =.029).

3.4. Discussion

In the present experiment, we explored the time course of the implicit processing of pain words, particularly whether the processing of a stimulus semantically associated to pain can help the individual to respond to an upcoming negative information in the environment. To our knowledge, our study represents the first to adopt the well-known affective priming paradigm combined with EEG recordings to investigate the neural correlates of the elaboration of pain words.

At the behavioral level, results replicated our previous findings illustrated in Chapter 2 using the same paradigm, confirming the affective priming effect both for positive and negative congruent conditions, in particular when the semantics of pain was considered in the analyses. ERPs findings allowed a deeper understanding of the underlying mechanism of this effect. At an earlier stage of stimulus processing, our data showed a significant effect on the N400 for the positive target with larger negativity when it is preceded by a negative prime (affective incongruency) rather than a positive one (affective congruency), in accordance to what had already been found in the literature (Eder et al., 2012; Zhang et al., 2006, 2010). Against our expectation, no effect has been detected for the negative target. Once the semantic of pain was entered in the analyses, it is interesting to see how the N400 component had larger amplitude when the positive target was preceded by a negative prime at posterior scalp positions rather than a positive prime or a pain prime. Again, no effect was found for the negative target. At first glance, at an early time window (300-500 ms), the semantic of pain is not playing any role in guiding the processing of upcoming information. Indeed, on the positive target, the N400 which primarily reads the semantic incongruency between stimuli is mainly elicited by a negative prime and not by a pain prime. Moreover, this effect was detected at the posterior scalp locations (Figure 4-5) restating previous findings of affective priming on words stimuli (Kissler et al., 2009; Zhang et al., 2010). This may also have depended by the visual modality of the stimuli (Eder et al., 2012; Kutas & Federmeier, 2011; Zhang et al., 2006) and, in particular, by the involvement of posterior areas during the perceptual analysis of word strings (Ponz et al., 2014).

At a later stage of stimulus elaboration, the affective incongruent conditions elicited a greater positivity on the LPP component for both positive and negative targets in agreement with previous studies on affective priming. Additionally, considering the semantic of pain it emerged that for the positive target, this effect was entirely driven by the pain prime: in fact, a positive waveform was elicited when a positive target was preceded by a pain prime but not by a negative prime. As well, a greater LPP was detected when the negative target was preceded by a positive prime rather than a pain prime. It is possible to speculate that the semantics of pain needs the allocation of more attentional resources to be elaborated, thus, influencing the subsequent response to a target information. It is well-known that a greater LPP is usually elicited by the inconsistency of valence due to the increased attentional resources (Kissler et al., 2009; Zhang et al., 2010). This component is indeed involved in tasks of attention, evaluation, and memory encoding (Kissler et al., 2009).

Considering that our study was the first to investigate the neural correlates of pain words using this paradigm, our findings need to be further interpreted. At an earlier stage (N400) of processing, the majority of ERPs studies on affective priming usually reported larger negativity in affectively incongruent conditions highlighting the sensitivity of the N400 to the semantic relatedness and congruency between the prime and the target (Eder et al., 2012; Steinbeis & Koelsch, 2011; Zhang et al., 2006, 2010). This might be read in the context of the spreading activation within the semantic network (Fazio et al., 1986; Murphy & Zajonc, 1993). Nevertheless, there is also additional evidence showing no effects (Herring et al., 2011; Kissler & Koessler, 2011) or even a reverse N400 effect (Aguado et al., 2013; Paulmann & Pell, 2010; Wang & Zhang, 2016) with a larger negativity for affectively congruent trials.

According to the literature, the N400 has also a role in the processing of integrating a target stimulus into the preceding context given by the prime. Embedding the target into the context may entangle two levels of affective evaluation: the first regards the elaboration of the valence, and the second regards the elaboration of the semantics of the stimulus (Aguado et al., 2013). The result of this dual evaluation turns out to differ for positive and negative emotional stimuli. For instance, a study by (Aguado et al., 2013) showed how a positive facial expression may be representative of several positive emotions so that it can be easily embedded within a large variety of positive target words. On the contrary, the integration of a target into a negative context (e.g., anger) requires the individual to distinguish among a broad range of emotional contents activated by negative valence stimuli. The high demands of this task may require the individual more time to be able to discriminate among the negative affective domain (Aguado et al., 2013). This may account for the inconsistency of results found in the literature regarding the affective priming for negative stimuli: the heterogeneity of the semantics embraced in the negative valence could have limited the emergence of the affective priming for the negative target (Rossell & Nobre, 2004). Nevertheless, it is worth pointing out that the semantics of pain needs more time to be elaborated on due to the necessity of additional attentional resources as a result of the specificity of the affective content that characterized it (Kissler et al., 2009; Zhang et al., 2010). This reaffirms the great sensitivity of the N400 discriminating the semantic content of the stimuli rather than just their valence.

However, at a later stage (LPP) of stimulus processing, the cognitive system is prepared to elaborate the evaluative properties of the stimuli generating peculiar effects according to the affective value of the stimulus (Herring et al., 2011). At this time, both positive and negative stimuli showed greater positive waveforms in the affectively incongruent conditions. Importantly, it is worth highlighting that these effects were entirely guided by the semantic of pain embedded in the prime: indeed, as soon as we considered it in the analyses, the LPP component resulted larger only when the positive target was preceded by a pain prime and not by a negative one. As well it is larger when the negative target was preceded by a positive prime rather than a pain one, and no significant effect was detected instead when the negative target was preceded by a positive prime rather than a negative one. These findings confirmed the involvement of the LPP during the processing of emotionally salient stimuli showing its role in generating a specific response to each type of emotion, in particular, it is clear how the effect on this component is due to the semantics of pain. Thus, if on one hand individuals are engaged in resolving the conflict between the semantics and the valence of a stimulus in the time window between 300 and 500 ms, then in the interval between 500 and 700 ms they are engaged in producing affective responses peculiar to each emotional content.

Besides positive and negative stimuli are differently processed in the brain, potentially due to the involvement of different brain areas (Comesaña et al., 2013), the relevance of considering the extreme heterogeneity of semantic contents among negative stimuli has largely been discussed in other previous studies on affective priming (Aguado et al., 2018; Gilioli, Borelli, & Pesciarelli, 2023; Rossell & Nobre, 2004). Indeed, pairs of words belonging to "fear" category generate a modest priming effect on negative targets (Rossell & Nobre, 2004). Conversely, pairs of words belonging to the "sadness" category produced an inhibiting effect on the processing of pain targets (Song et al., 2019). It follows that affective categories within negative valence should be considered separately, which is why results are so inconsistent (Aguado et al., 2013; Eder et al., 2012; Herring et al., 2011; Paulmann & Pell, 2010).

In addition, another limitation of our experiment was the recruitment of a sample composed only by females. Indeed, other studies reported gender differences using this particular paradigm, with stronger effects in female than male participants (Aguado et al., 2013; Eder et al., 2012; Herring et al., 2011; Paulmann & Pell, 2010). Moreover, gender differences have been extensively covered by studies on pain processing (Rhudy & Williams, 2005). Much research has shown that females reported more intense reactions to pain stimuli (Rhudy & Williams, 2005), and even a different perception of risk than males (Charness & Gneezy, 2012). Based on these differences and our previous study using the same paradigm (Gilioli, Borelli, & Pesciarelli, 2023), we initially preferred to focus on females to maximize a possible effect, but for generalizability of the results, there is the need to extend the study to males.

To sum up, the ERPs components analysis gave a novel insight on the time course of the implicit processing of pain. It appears that the time window between 300 and 500 ms is crucial to studying the interaction between the semantics and the valence of a stimulus. Furthermore, the findings emphasise the importance of considering the semantics of negative stimuli. In fact, at this time, the semantics of pain of the prime required the allocation of more cognitive resources to be elaborated among the heterogeneous groups of emotional contents of negative stimuli. The more the stimulus processing progresses in time, the more the cognitive system is able to recognize the adaptive value of the pain content pre-activating the individual to respond as quickly as possible to un upcoming negative information, as behavioral findings showed. Indeed, the time window between 500 and 700 ms turns out to be extremely sensitive to generate specific responses to each affective and emotional information. As already stated by (Herring et al., 2011), we can speculate that the N400 is more sensitive to the evaluation of the semantics of stimuli and the LPP to their affective evaluation.

Ultimately, it is possible that the double nature of pain itself may have contributed to generating this complex pattern of results. According to the motivational priming theory (Herring et al., 2011), pain has specific properties, and its elaboration may promote the survival of the individual both by facilitating the individual to respond faster to aversive signals, both by supporting approach responses to others' pain.

However, individual differences in pain processing may account for the effect as showed by correlation analyses. In particular, on behavioral results, the correlation of the affective priming and the Magnification subscale of the PCS suggested that the individual tendency to amplify the severity of negative stimuli may have influenced the response to the target. In particular, the correlation between the negative priming associated to pain prime and the Perspective Taking subscale of IRI proposes a relation with the capacity of feeling compassion for others. On ERP results, the N400 elicited by the negative prime on the positive target might have been influenced by the tendency of an individual to respond to threat signals (BIS scale) and to feel personal distress (IRI Personal Distress subscale).

On the other side, the LPP on the negative target correlated with the tendency of the individual to get involved in vivid and imaginative fantasies (IRI Fantasy subscale). Both the N400 and the LPP seemed to be impacted by the tendency of an individual to ruminate about negative thought (Rumination subscale of PCS). The individual influences on the affective priming related to pain prime especially on the LPP restated that the role of the component in the elaboration of emotionally salient stimuli can be top-down modulated by the subjective interpretation of the stimuli (Hartigan & Richards, 2016).

In the present study, the category of negative, pain-unrelated words included words belonging to different semantic contents. In future studies, it would be of interest to compare pain-related words to other defined semantic categories, like other negative emotions, as they may represent more appropriate comparisons. However, not all words may be unambiguously categorized into a discrete emotion or a specific semantic content, raising concerns about statistical power (Kveraga et al., 2015; Witherell et al., 2012). Defining an appropriate paradigm, experimental design, normative data, and statistical analysis are crucial aspects that researchers should carefully consider avoiding this potential problem. For instance, a paradigm that includes contextual information to aid the disambiguation of semantic content may be useful for better accuracy. Collecting normative data may also help categorize the semantic content of each stimulus and prevent extraneous sources of variation.

In conclusion, this study represents the first data on the topic. Despite cautious interpretation of ERPs results is needed- they do not survive correction for multiple comparisons- it provides a small contribution to studying the process of sensorimotor resonance between oneself and others, also called empathy. This will allow to understand the other through the vicarious sharing of their emotional experiences and beliefs (Betti & Aglioti, 2016).

Chapter 4

The role of semantic relatedness in predicting the emotion concept organization using an emotion fluency task in older adults

4.1. Introduction

So far, my studies on affective priming have focused on the automatic processing of the affective and semantic content of an emotional stimulus during its perception. Once the cognitive system detects a stimulus in the environment, it stores the embedded information in semantic memory. When individuals want to access and retrieve emotional information, they need to voluntarily search through the semantic memory for the appropriate stored units that may not have been activated in the initial and automatic spread of activation. To study how the affective and semantic valence of a stimulus influence the way in which individuals voluntarily access semantic memory, we decided to use an emotion fluency task, which requires intentional retrieval of emotion concepts from memory.

In everyday life, we use emotion words to parse our emotional experiences, a process that requires the selection and retrieval of emotion concepts from our semantic memory (Hegefeld et al., 2023). According to associative network theory, emotion words are nodes within a semantic network, and each emotion word reflects an abstract verbal symbol associated with an underlying concept (Bower, 1981). People have different conceptual knowledge of the same emotion words, which enables them to organize and recall emotion concepts (Hegefeld et al., 2023). Few studies have employed fluency tasks to comprehend how concepts are stored in memory (Ford et al., 2012; Libkuman et al., 2004). Here, we used an emotion fluency task (i.e., how rapidly individuals can produce words related to emotions) to investigate how emotion concepts are organized in semantic network based on their valence and semantic connections.

Grounded in the associative network theory, affective priming studies have shown how positive and negative information are organized differently in memory and elicit distinct behavioral and neural responses. The activation of a node in the semantic network facilitates the activation of all associated nodes (*spreading activation theory*- Fazio et al., 1986; Murphy & Zajonc, 1993) and this holds true for affective stimuli: presenting a positive prime facilitates the response to a positive target compared to a negative one. Positive and negative primes have a different influence on target processing due to the distinct organization of emotional material in memory (Bower, 1981). Valdivia-

Moreno et al. (2023) proposed that emotion fluency, which demonstrates how people move through semantic network, can provide insights into the structure of emotion concepts in semantic memory.

Despite the paucity of studies using the emotion fluency task in the literature (Abeare et al., 2017; Camodeca et al., 2021; Galli et al., 2005; Gawda, 2019; Gawda et al., 2017; Gawda & Szepietowska, 2013; Hegefeld et al., 2023; Lam & Marquardt, 2020; Rossell, 2006; Sass et al., 2013; Schrauf & Sanchez, 2004; Tabert et al., 2001; Valdivia-Moreno et al., 2023; Wauters & Marquardt, 2018; Yeung, 2022; V. Zammuner & Galli, 2001; V. L. Zammuner, 2011), some of them have found a consistent positivity bias in emotion fluency tasks with individuals generating more positive than negative words (Lam & Marquardt, 2020; Sass et al., 2013; Tabert et al., 2001; Wauters & Marquardt, 2018). The positivity bias is attributed to differences in storage and processing of positive and negative words, with positive words acquired earlier in time (Ponari et al., 2018) and showing more detailed elaboration in memory (Sylvester et al., 2016; Unkelbach et al., 2008). Indeed, it has been shown that the emotional valence of words is positively correlated with the number of word associations- the more positive a word is, the greater the number of words associated with it (Hofmann & Jacobs, 2014). Moreover, the inherent lexical and semantic differences between positive and negative words may contribute to this effect: positive words are usually more familiar (i.e., higher frequency), more dominant (i.e., denoting something that is stronger), and more concrete (i.e., easier to picture) than negative words (Valdivia-Moreno et al., 2023). In contrast, the complexity of the emotion concepts within the negative domain contributes to the more intricate organization of negative information (Rossell & Nobre, 2004).

Only a few studies have identified a *negative* bias, where individuals generate more negative words than positive in the emotion fluency task (Hegefeld et al., 2023; Schrauf & Sanchez, 2004; Valdivia-Moreno et al., 2023; V. L. Zammuner, 2011). This tendency may be attributed, in part, to the abundance of negative emotion words in English compared to positive or neutral terms, as highlighted by (Jackson et al., 2022). It been observed that negative words tend to have higher arousal than positive ones, making them more likely to draw people's attention (Võ et al., 2009). In this regard, age and sex may play a role in the way in which people search for and attend to emotions words in the semantic memory: a negativity bias can be more pronounced in childhood and decrease gradually across age groups (Valdivia-Moreno et al., 2023) with women showing a higher tendency toward negative affect than men (Gawda & Szepietowska, 2013).

One of the reasons for these heterogeneous results may lie in the degree to which emotion words are related in semantic memory, also referred to as "semantic cohesion" (Tulving & Pearlstone, 1966). Experiments on affective priming have already demonstrated that the processing of emotion words is not only affected by their valence, but also by their semantic content, leading to specific emotional responses (Gilioli, Borelli, Serafini, et al., 2023). Beyond the valence bias, emotion fluency tasks provide an opportunity to explore the lexical and semantic dimensions of words that structure the order in which emotion words spontaneously come to mind. In their recent study, Valdivia-Moreno et al., (2023) established that valence, dominance, and concreteness could predict the order of words produced by the participants so that words produced later in the task tended to be more positive, less dominant, and less concrete. Currently, no research has investigated the role of semantic relatedness between emotion words as a predictor of word order. Since semantic relatedness can improve memory performance by narrowing down search parameters during word retrieval (Buchanan et al., 2006), it might be worth considering when analyzing the emotion fluency task as it may offer insight into the properties of words that arise first.

The goal of this study was to further investigate the structure of the semantic memory of emotions by investigating the psycholinguistic properties of words generated in the emotion fluency task. As the first goal was to validate the emotion fluency task as a valuable tool, we compared emotion fluency scores to fluency measures from other semantic domains, such as food and body parts. Then, we tested whether there was a positivity bias to provide clarity to the ongoing debate and to include a control condition that could account for the arousal categorization of the words. The analysis of the valence of the words that were produced may unveil aspects of an individual's emotional experiences and be an indicator of emotional functioning (Camodeca et al., 2021). Finally, we explored lexical parameters that could predict the order in which the words were spontaneously generated during the emotion fluency task. The uniqueness of this study was that we investigated the role that semantic relatedness had in shaping the order of words generated during the task. This will represent a further support of the intimate relationship between emotions and semantics.

4.2. Methods

4.2.1. Participants

Forty-three healthy older adults (26 females- aged 23-88 years) participated in the present study, among which 19 were volunteers in the Hillblom Healthy Aging Network, a longitudinal study of healthy aging at the University of California, San Francisco (UCSF), and 24 were unaffected family members of patients with frontotemporal lobar degeneration enrolled in two multisite genetic FTD research projects, the Advancing Research and Treatment for Frontotemporal Lobar Degeneration (ARTFL) and Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS).

All participants underwent an extensive, multidisciplinary team evaluation that included a clinical history, neurological examination, neuropsychological testing, and informant-based functional interview. Participants completed the Mini-Mental State Examination (MMSE), a brief screen of cognitive functioning (Folstein et al., 1975) and all scored 27 (out of 30) or higher. The study procedures were approved by the UCSF Committee on Human Research, and all participants provided written informed consent. Participants were financially compensated for their participation.

4.2.2. Procedure

All data from this study were collected at a single in-person or remote laboratory session between 2022 and 2023. Participants were required to perform three tasks of verbal fluency in which they were given 60 seconds to name aloud as many words as possible belonging to a category. The categories in questions were respectively: emotions and feelings (Abeare et al., 2017; Camodeca et al., 2021), foods and drinks (John et al., 2018), and body parts (Berto & Galaverna, 2016). Participants' responses to all conditions were recorded as audio files and later transcribed. The emotion word fluency test (EWFT) is a measure of emotion word production where participants are asked to give as many emotions words as they can within one minute (Abeare et al., 2009; Abeare et al., 2017; Camodeca et al., 2021).

4.2.3. Scoring

4.2.3.1. Non-emotion verbal fluency tasks

As control tasks, we used two non-emotion verbal fluencies, assessing different semantic categories: (1) foods and drinks and (2) body parts. Food category usually encompass concrete words easy to retrieve compared to emotions words (Papagno, 2022). Body parts instead represent a special category that falls between food and emotions. It embeds concepts less abstract than emotions but that can be referentially keyed naming the person's own body and sensory-experienced as emotions (Berto & Galaverna, 2016).

The responses were scored by two independent research coordinators. For each participant, we computed a total score for each of the two verbal fluency categories (food/drinks, body parts) by calculating the total number of valid and distinct words produced for that category. Responses not part of the category of interest were scored as rule violations. Repeats of the same exact word were scored as a repetition. Items that were difficult to transcribe due to poor audio quality were marked as unscorable.

4.2.3.2. Emotion fluency task

To create a total emotion fluency score with high reliability, we scored participants' responses according to published affective lexicons of emotion words (Ortony et al., 1987; Shaver et al., 1987). Any responses included in these lexicons were scored as correct. Responses that were of a different form but of the same root as that included in the lexicon were scored as correct (e.g., "cheery" was scored as correct despite not being included in the lexicons because "cheerful" was included). Again, as above, repeats of the same root were not scored as repetitions and a point was given for each. Responses not included in the lexicons in any form were scored as set losses. Accordingly, for each participant, we computed a total emotion fluency score by calculating the number of valid and distinct emotion words each participant produced.

4.2.4. Data processing

Descriptive statistics (e.g., mean, standard deviation) of non-emotion verbal fluencies and emotion fluency scores were computed.

Data were processed generating three distinct datasets: (1) a subject-level dataset to compare the performance of the participants across semantic categories; (2) a subject-level dataset only on emotion fluency task where we tested the positivity valence bias using the valence categorization labels and additionally the arousal categorization labels; (3) a word-level dataset that linked each word produced in the emotion fluency task to the relevant psycholinguistic parameters to examine whether valence, arousal, and the semantic relatedness of the word generated predicted the order in which the emotion words were produced . For each participant, the order in which all the words were produced was noted. This order was only analyzed for valid emotion words within each category, but order was assigned in relation to all words a participant produced. For example, if a participant produced the words "happy" (emotion), neutral (non-emotion), and excited (emotion), we recorded the order placement of all three words, such that happy would receive a word order placement of 1, neutral would be 2, and sad would be 3. Consequently, our analyses only examined relations between lexical parameters and correct words (i.e. in this example, "neutral" would not be analyzed).

4.2.4.1. Valence and arousal categorization of emotion words

Given that people usually refer to their own emotions using labels such as positive and negative emotion, for each participant we labelled the words that fell below from the mean valence as negative and the ones above 0.5 as positive. We then computed the proportion of positive and negative words for each participant.

For each participant, we also labelled the words that fell below from the mean arousal as low arousal and the ones above 0.5 as high arousal. We then computed the proportion of low and high arousal words for each participant. Consequently, we were also able to calculate the overall proportion of high and low arousal positive words, and the proportion of high and low arousal negative words for each participant.

4.2.4.2. Psycholinguistic measures of emotion words

For word order analyses, we combined data from several large corpora to produce a dataset that connected the valence, arousal, dominance, concreteness, familiarity, and semantic relatedness of words produced in the task. However, some emotion words did not have exact matches in these norming corpora. For these words, we first combed through each lexicon to find the closest available matches (e.g., "peaceful" for "peacefulness") and used these as substitutions.

The affective measures of valence, arousal, and dominance were derived from lexical norms compiled by Warriner et al. (2013), which provide normative ratings for each of these dimensions that vary from 1-7, where higher scores indicate greater positive valence, arousal, and dominance. The affective measures of concreteness and familiarity (*word prevalence score*) were derived by (Brysbaert et al., 2019). These norms were established by taking the mean of participant ratings for those variables. We paired these values with participant response words on the three fluency tasks.

The semantic relatedness between a pair of words were calculated using the *Wup* similarity measure (Wu & Palmer, 1994) in WordNet::Similarity library software (Pedersen et al., 2004), as explained in Study 2.

Normed ratings were not available for 5.6% for valence, arousal, and dominance; 2.55% for concreteness, and 1.16% for familiarity. Valid substitutions were found for 0.47% of words for valence, arousal, and dominance; 1.23% for concreteness and 1.1% for familiarity.

4.2.5. Statistical analyses

Analyses were conducted only on correct words using R through *JAMOVI* (version 2.3), which provides a good graphical user interface, and R studio (version 2023).

4.2.5.1. Comparing emotion fluency and non-emotion verbal fluencies

We first performed Pearson's correlations between the emotions, food, and body parts scores (total number of correct words) and correcting for multiple comparisons. We hypothesized that emotions, food, and body parts fluency would be positively correlated with each other.

4.2.5.2. Examining valence and arousal

a. *Correlations with age, education, and gender*

We first tested for the presence of any associations with control variables using two Pearson's correlations by relating the total number of positive and negative words produced with age and education. We checked for gender differences using a simple t-test.

b. *Testing the positivity bias using valence and arousal categorization labels*

We conducted a one-way ANOVA to compare the proportion of words produced across each valence category (positive and negative). We hypothesized that positive words would be produced at a higher rate than negative words, according to a previous study (Sass et al., 2013).

We performed a repeated measures 2x2 ANOVA (valence: positive, negative – arousal: high, low) to test the interaction between the arousal and the valence on the proportion of words produced. We hypothesized arousal would play a contributing role in the fluency tasks such that high arousal words would be produced more than low arousal words. In addition, we expected an interaction effect between the arousal and valence of the words.

4.2.5.3. Testing the word order predicted by valence, arousal, and semantic relatedness

To address our third research question, based on Valdivia-Moreno et al., 2023, we performed three distinct mixed-effects models, one for each predictor using the *lme4* (version 1.1.27.1; Bates et al., 2015) and *clmm* in *ordinal* packages (version 2022.11.16) to account for ordinal dependent variables. The predictors were valence, arousal, and semantic relatedness.

To compute these analyses, we used the word-level dataset created as explained in paragraph 4.2.4.2. In these models, the word order in which each emotion word was produced represented the outcome variable, each predictor was included as a fixed factor, and the participant ID as a random effect to nest words within participants. These models were built to examine which predictors were related to the word order. Finally, a final mixed-effects models was performed using all the three predictors together with the other psycholinguistic measures such as concreteness, dominance, and familiarity.

4.3. Results

4.3.1. Comparing emotion fluency with non-emotional verbal fluencies

Descriptive statistics for non-emotional verbal fluencies and emotion fluency tasks are shown in Table 1.

Pearson's correlations among the total correct words for the three fluency measures (emotions, food, body parts) showed a significant correlation between food and body parts (Pearson's r = 0.592; p_{Bonf} <.001) and between emotions and body parts (Pearson's r = .44; p_{Bonf} = .003). No significant correlation was found between food and emotions (p > .05).

Table 1. Verbal fluency task results: mean and standard deviation for the proportion of correct words, concreteness, and familiarity measures across categories.

Category	Proportion correct words **Mean (SD)**	Concreteness **Mean (SD)**	Familiarity **Mean (SD)**
Food	38.3 (± 5.2)	4.8 (± 0.06)	6.25 (± 0.09)
Body Parts	42.2 (± 3.9)	4.78 (± 0.05)	6.28 (± 0.04)
Emotions	19.3 (± 3.5)	2.34± (0.15)	6.34 (± 0.08)

4.3.2. Examining valence and arousal

a. Correlations with age, education, and gender

Pearson's correlations showed a marginally significant positive correlation between positive words and age (Pearson's r = .296, p= .054) and a marginally significant negative correlation between negative words and age (Pearson's r = -.292, p= .058). By a visual inspection, the data suggested a possible non-linear relationship between the total number of positive and negative words and age. When tested for a quadratic relationship, the number of negative words showed a significant quadratic relationship with age [F (1, 41) = 4.49; p = .042] and the number of positive words showed only a tendency toward a quadratic relationship with age [F (1, 41) = 3.54; p = .06] although it did not reach statistical significance. No effect for education or gender was detected.

b. Testing the positivity bias using valence and arousal categorization labels

Descriptive statistics for valence and arousal are shown in Table 2.

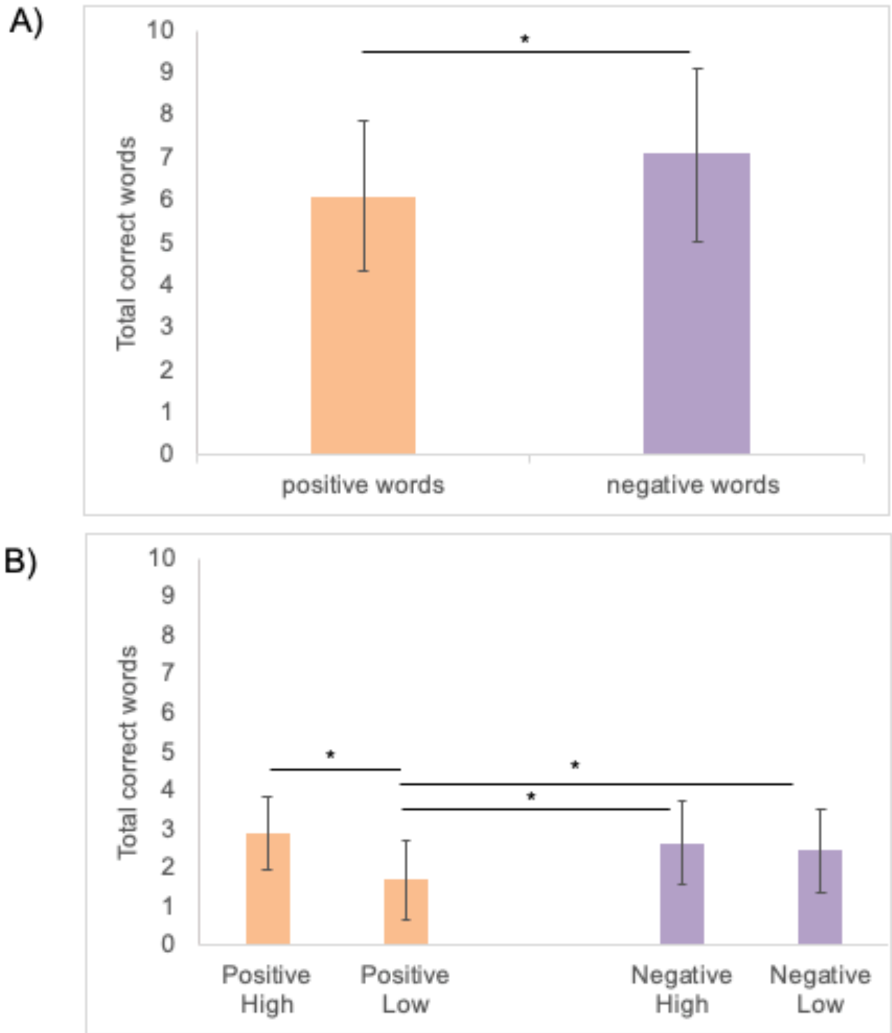
The repeated measures ANOVA with valence (positive and negative) as a factor showed that participants produced more negative words than positive words [F (1, 42) = 5.33, p = .026] (Figure 1.A)

The repeated measures 2x2 ANOVA for valence and arousal showed a significant main effect of arousal where high arousal words were produced with higher rates than low arousal words [F (1, 42) = 64.29, p = <.001]. A significant valence x arousal interaction was reported [F (1, 42) = 6.25, p = .016], and post hoc comparisons showed that participants produced more positive arousal words than positive low arousal words [t (42) = 5.44, p_{holm} = <.001] and negative low arousal words [t (42) = 2.42, p_{holm} =.056]. Additionally, participants produced fewer positive low arousal words compared to negative high arousal words [t (42) = 4.84, p_{holm} <.001] and low arousal words [t (42) = -2.79, p_{holm} = .027] (Figure 1.B).

Table 2. Emotion fluency task results: mean and standard deviation for the total number of positive and negative words with high and low arousal.

		Valence		
		Positive	**Negative**	*Total Arousal*
Arousal	High	2.9 (±0.96)	2.7 (±1.09)	5.7 (±1.28)
	Low	1.7 (±1.01)	2.4 (± 1.1)	4.4 (±1.18)
	Total valence	6.1 (±1.8)	7.1 (± 2.03)	

Figure 1. Emotion fluency task results: A) Analysis on valence categorization labels: higher rate of negative words than positive words. B) Analysis on the interaction effect between valence categorization and arousal categorization labels: positive words with high arousal had higher rates than positive words with low arousal. Negative words with high and low arousal had higher rates than positive words with low arousal. Significant comparisons are marked with *.



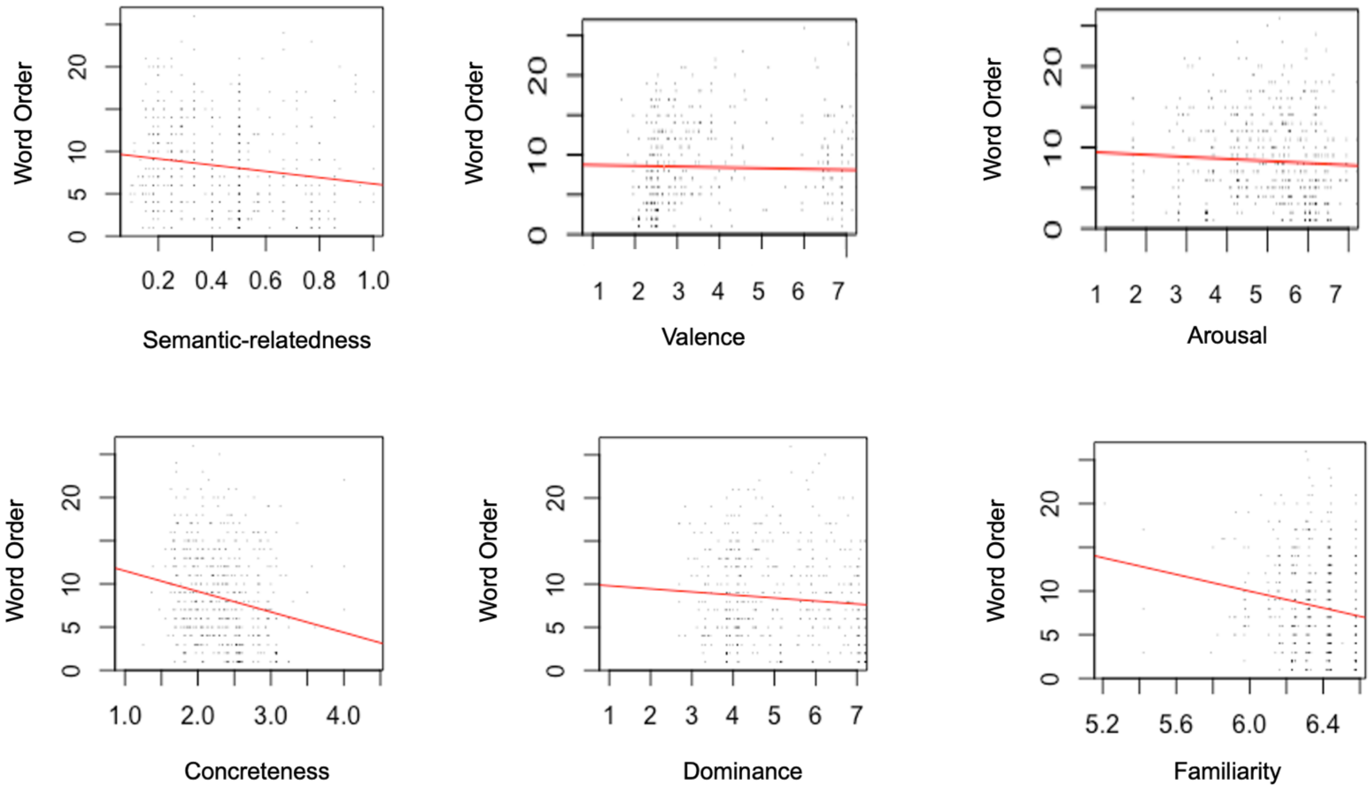
4.3.3. Testing the word order predicted by valence, arousal, and semantic relatedness

We used three mixed-effects models to test which lexical parameters were associated with word order. These analyses revealed that only semantic relatedness [$\beta = -1.59$, $z = -3.94$, $p < .001$] was a significant predictor of word order. Words produced later in the emotion fluency task tended to be less semantic related. Valence was not a predictor of word order [$\beta = -0.04$, $z = -1.22$, $p = .223$] or arousal [$\beta = -0.1$, $z = -1.69$, $p = .091$].

An additional mixed-effects model tested which lexical parameters were associated with order when controlling for all other psycholinguistic parameters, also embedding concreteness, dominance, and familiarity. This analysis revealed that semantic relatedness [β = -1.65, z = - 4.07, p < .001] as well as concreteness [β = -0.95, z = - 5.04, p <.001], dominance [β = -0.31, z = - 2.28, p = .023] and familiarity [β = -1.64, z = - 3.36, p < .001] were predictors of word order. Words produced later in the emotion fluency task tended to be less semantic-related, less concrete, less dominant, and less familiar.

All the predictors are shown in Figure 2.

Figure 2. Scatterplot showing the results from mixed-effects models to test the psycholinguistic predictor of the word order in the emotion fluency task. Semantic relatedness, concreteness, dominance, familiarity predicts the order the words come to mind (p < .005).



4.4. Discussion

The present study was aimed at delving into the organization of semantics of emotions by exploring the psycholinguistic characteristics of words produced in an emotion fluency task. Overall, emotion fluency was tested as a good measure of semantic fluency due to its correlation with body parts fluency. In general, our results showed that participants produced more negative than positive words and that this negativity bias has a non-linear relationship with age. More interestingly, we were able to see an interaction between arousal and valence especially for positive words: indeed, positive words with high arousal words produced more than positive words with low arousal. This effect was not found in the negative domain. Finally, we investigated the structure of the semantic memory of emotions by testing the psycholinguistic predictors of the order in which participants produced words. Results showed that semantic relatedness was a significant predictor of word order, even when controlling for other lexical variables such as concreteness, dominance, and familiarity. This suggests emotion fluency is a specific subset of verbal fluency. Taken together, these results offer new insights into the key dimensions with which emotional concepts are organized in memory.

Emotion fluency represents a unique category to address the issue and the correlation with body parts suggests - their intrinsic nature in capturing body sensations and feelings, which implies interoceptive processes (Berto & Galaverna, 2016). Our main question was to investigate the positivity bias that had been found in the literature (Lam & Marquardt, 2020; Wauters & Marquardt, 2018), which assumes that positive words share more associations in semantic memory than negative words because they are stored differently. What we found instead, however, was a negativity bias. Although positive words offer inherent advantages in their nature and in the way the individual imagines them in memory, negative information is known to have more impact on the expression of attitudes and behaviors (Ito et al., 1998). Negative stimuli have an evolutionary significance for human survival and immediately activate the autonomic fight-or-flight response (Ito et al., 1998). Negative stimuli may contain more informational value than positive stimuli and, thus, take priority in semantic memory processing. The fact that we found this effect not only in priming but also in a fluency task suggests that the negativity bias operates not only on an automatic level but also on a conscious level. This reinforces the adaptive advantage of the negative valence of a stimulus (Ito et al., 1998).

According to the circumplex model, we added arousal, which it is known to play a role in the way an individual stores information, to the valence analysis. Results showed that overall high arousal emotion words are more salient and, therefore, produced with the highest frequency. Most importantly, the role of arousal seems to interact with valence for positive words, but not for negative ones. Indeed, positive words with high arousal are produced more than positive words with low arousal. It is well known that arousal plays a key role in the way individuals store information in memory. However, it is unclear whether it facilitates or interferes with retrieval performance. Generally, it has been seen that negative information is retained in memory over time regardless of arousal (Christianson, 1992). It is therefore possible that our task arousal has favored the production of positive information, which is retrieved more easily when it is more salient. On the other hand, negative information has an intrinsic activation value due to its evolutionary relevance for survival and did not suffer from the effect of arousal.

In addition to the analysis of valence, guided by the previous literature (Valdivia-Moreno et al., 2023), we also examined how the order in which participants generate emotion words can reveal the structure in which emotion concepts are stored in memory. We hypothesized that the circumplex model's dimensions, especially valence and arousal, would help to explain the word order. What previous studies had not yet considered was a measure of how emotion words were closely related and differentiated from other concepts in semantic memory. As mentioned in the introduction of the thesis, it is worth accounting for the subtle but important difference between affective valence and semantic valence as a third dimension (Itkes & Kron, 2019). We thus introduced as a predictor the semantic relationship between the words produced in a sequence. The results partially supported our hypothesis: contrary to what we expected, voluntary and conscious retrieval of emotional information in memory is not driven by valence, or arousal, but by the semantic relationship shared by consecutive produced words. In fact, the single regression models for each predictor did not report significant results either for valence or arousal. On the contrary, the semantic relatedness of the words produced was a robust predictor, even when controlling for other psycholinguistic variables such as concreteness, dominance, and familiarity. Words produced at the beginning of the fluency task were words with a stronger semantic relationship and words that were more concrete, dominant, and familiar. The advantage of semantic relatedness in memory was already highlighted by prior studies on verbal memory (Buchanan et al., 2006; Tulving & Pearlstone, 1966). Our findings suggest that during the voluntary retrieval of emotional information, individuals firstly relied on the so called "semantic-valence" to reduce the search parameters in the retrieval.

These results suggest that when we have to recover emotional information from memory in a voluntary way, we first rely on the so-called "semantic-valence," which is the factual knowledge about the valence of an object, instead of the "affective valence," which is the pilar of automatic processes as we have seen in affective priming (Gilioli, Borelli, & Pesciarelli, 2023; Gilioli, Borelli, Serafini, et al., 2023). When individuals are called upon to actively retrieve emotional information from memory, they tend to choose words that are closely related in the associative network, parsing one concept from another. Often, performance on memory tasks is enhanced by a combination of arousal and semantic relatedness (Buchanan et al., 2006; Maratos et al., 2000; Talmi & Moscovitch, 2004). Although we found a significant effect of arousal by comparing high and low arousal words and also an interaction with valence, our regression model did not recognize it as a predictor of word order. This finding is consistent with the results of Valdivia-Moreno et al. (2023)who also did not find any effect for arousal. One reason that can potentially explain these null effects is that our sample size was not large enough to perform a word-level analysis. Indeed, this limitation is important as the computation of the semantic relatedness itself was not available for all word pairs, resulting in a loss of data in analyses for other variables such as valence and arousal.

Ultimately, our study relied on an exemplar dictionary of emotions that was based on the early studies of the affective lexicon (Ortony et al., 1987; Shaver et al., 1987). This highly systematized tool strengthens our results that highlight the role of semantic relatedness, more than valence, in organizing the structure of emotions in memory. Indeed, ERPs results in Gilioli, Borelli, Serafini, et al. (2023) have shown that affective valence evaluation requires a deeper analysis of the stimulus, which happens at a later stage of stimulus evaluation. This reinforces the notion that the voluntary retrieval of emotional concepts from memory mostly relies on semantic valence. Future studies can delve into the brain correlates of this process to help the ongoing debate on the hemispheric lateralization of emotions. The negativity bias might support the existence of distinct neural connections that characterized the heterogeneous semantic content within the negative domain. Exploring the gradient of emotions within each domain and their neural correlates in healthy and pathological brains can reveal the structure of the semantics of emotion.

Chapter 5

"I'm Sending You Healing Magic": Right Anterior Temporal Lobe Atrophy Relates To Elevated Positive Emotion, Mysticism, And Religiosity In Semantic Dementia

5.1. Introduction

Up to this point the thesis has examined the behavioral and temporal course of affective and semantic processing of emotions in healthy individuals. In the literature, there is an ongoing debate about the hemispheric lateralization of socioemotional knowledge in the brain. It is not clear whether the right hemisphere is dominant in processing emotional information independently of its valence or, on the contrary, whether it is dominant in processing negative information and the left hemisphere in processing positive information. To shed light on the neuroanatomical substrates of affective and semantic processing, we decided to study the behavioral and emotional changes in a group of people with emotional dysfunctions, such as those with semantic dementia.

In semantic dementia (SD), a neurodegenerative disorder characterized by asymmetric frontal and anterior temporal lobe atrophy, people often exhibit elevated positive emotional reactivity and experience as well as other changes in behavior (Shdo et al., 2022).

SD manifests in two clinical variants: the semantic variant of primary progressive aphasia (svPPA), which is characterized by left ATL atrophy that results in loss of verbal and object-related semantic knowledge (Gorno-Tempini et al., 2011; Lambon Ralph et al., 2010); and the semantic behavioral variant of FTD (sbvFTD), which is characterized by right ATL atrophy that results in loss of socioemotional semantic knowledge and empathy and in the emergence of compulsions and rigidity (Younes et al., 2022). Despite distinct diagnostic profiles, both syndromes may include changes in behavior and emotions, although these may differ considerably depending upon the predominant side of involvement (Edwards-Lee, 1997). In the early stages of disease, changes in behavior and emotions are more common in sbvFTD (Edwards-Lee, 1997; Vonk et al., 2020; Younes et al., 2022), which highlights the important contribution of the right ATL to socioemotional behaviors (Olson et al., 2007).

While semantic knowledge impairments in SD are well documented, less is known about the associated behavioral and emotional changes (Chan et al., 2009; Gorno-Tempini et al., 2004; Hua et al., 2023). The limited available data, which mostly come from individual case studies in SD, suggests behavioral and emotional changes are multifaceted (Chan et al., 2009). Personality changes (Mendez, 2018; Miller et al., 2001) such as expansive or euphoric mood (Block & Miller, 2019; Ohm et al., 2023), eccentricity (Edwards-Lee, 1997), and grandiose delusions (Naasan et al., 2021; Shad et al., 2019) as well as abnormal social interaction, ‘bizarre affect’ (Thompson et al., 2003), and childlike behavior (Chan et al., 2009) have been documented in various case reports. Individuals with predominantly right-sided ATL atrophy may undergo profound shifts in their sense of self, which can alter various aspects of their lives such as political orientation, fashion preference, career choice, philosophical viewpoints, sexual behavior, and religious beliefs (Block & Miller, 2019; B. L. Miller et al., 2001; Ohm et al., 2023). They may experience a perceived dissolution of the boundaries between self and other and a sense of union with something larger than oneself (Miller et al., 2019). Individuals with right-lateralized ATL damage often experience a feeling of sense of connectedness with natural and supernatural words (Block & Miller, 2019), a construct with a deep history in psychological research (Arumugam, 2015; Watts et al., 2022). In the literature, these experiences have also been defined as mystical or spiritual such as these individuals appear to have embraced a sense unity with the world (Miller et al., 2019), a sense of sacredness (Arumugam, 2015) or have encountered the “ultimate reality” (Arumugam, 2015). Overall, such experiences are usually described as evoking positive feelings such as happiness, blissfulness, peace, and joy (Arumugam, 2015).

Despite their initial focal atrophy on the left ATL that leads to prominent language deficits, people with svPPA can also exhibit increased mood (Shimizu et al., 2011), heightened social interest (Mendez et al., 2006; Snowden et al., 2001; Sturm et al., 2011), and elevated expressions of positive emotions (Kumfor et al., 2019; Shdo et al., 2022). This suggests a potential elevation of certain positive emotions also in svPPA, but without necessary exhibit profound changes in the sense of self or mystical and spiritual experiences. It might be attributed to the spreading of the disease to the contralateral hemisphere, involving the right ATL, ventral anterior insula, and orbitofrontal cortex (Collins et al., 2017; Guo et al., 2013; Landin-Romero et al., 2016; O’Connor et al., 2016; Seeley et al., 2005).

Together with changes in behavior, people with SD show impairments in emotion processing including difficulties with recognizing (Kumfor et al., 2016; Rosen, 2002), expressing (Pressman et al., 2023), and regulating (Shdo et al., 2022; Sturm et al., 2015) emotions. Although these deficits in emotion processing seem to be more prominent in individuals with right-lateralized atrophy (Irish et al., 2014; Kumfor et al., 2016; Perry et al., 2001; Rankin et al., 2006), they also occur in those with left lateralized atrophy (Irish et al., 2013; Rosen, 2002; Shdo et al., 2022; Sturm et al., 2015). Functional neuroimaging studies on healthy individuals have suggested that the two hemispheres play a distinct role in processing stimuli of differing emotional valence such that the left is dominant for positive information and the right is dominant for negative information (Canli, 1999). Research on individuals with FTD show reduced understanding and emotional reactions to negative emotions in individuals with right-lateralized atrophy in the frontal and temporal lobes (Eckart et al., 2012; Hua et al., 2019; Rankin et al., 2006; Rosen, 2002; Sturm et al., 2006). Atrophy in the right ATL (Irish et al., 2013) and right amygdala (Rosen, 2002) is also associated with impaired negative emotion recognition. On the other hand, the degeneration of the left hemisphere of the brain can impact the functioning of emotion regulation systems, including the inferior frontal gyrus and dorsal anterior insula, and it can result in dysregulation of positive emotions (more smiling behavior) (Shdo et al., 2022; Sturm et al., 2015). This suggests that atrophy in the emotion regulation systems centered in the left hemisphere may "release" emotion generator systems and accentuate positive emotional reactivity (Shdo et al., 2022; Sturm et al., 2015, 2018). As such, the study of SD offers an opportunity to deepen into the longstanding debate on the hemispheric lateralization of emotions, especially investigating the role of the right ATL in generating the positive feelings associated to a sense of connectedness with the self and the world.

Historically, the first attempts to define the neural correlates of religious and mystical experiences came from patients with temporal lobe epilepsy (Geshwind, 1983). People with right temporal lobe epileptic foci (Brooks & Hoblyn, 2005; Devinsky, 2000; Devinsky & Lai, 2008; Geshwind, 1983) showed an intensification of religious and mystical experiences Similarly, people with a traumatic brain injury in the dorsolateral prefrontal cortex and right middle/superior temporal cortex reported greater mystical experiences (Cristofori et al., 2016), elated mood such as mania (Jorge & Arndt, 1993; Mesulam, 2023), or feeling that they had a special power (Brooks & Hoblyn, 2005). These findings suggest that the frontal and temporal lobes may play a role in the experiential aspects of religiosity, including mystical and spiritual experiences, and that the right hemisphere may have a unique involvement in experiences related to the corporeal, emotional, and spiritual self (Block & Miller, 2019).

The right ATL serves as a core hub in the semantic appraisal network, linking the semantic concepts with personalized emotional evaluation and leading to a more accurate comprehension of social and emotional cues (Rankin, 2020). People with sbvFTD show greater right ATL atrophy, an area important for emotion recognition (Kumfor et al., 2016) and other socioemotional abilities (Perry et al., 2001; Rankin et al., 2006). Indeed, the right ATL is responsible for assigning valence to stimuli, especially negative ones (e.g. disgust, fear) (Canli, 1999). Damage to this area can lead to an increase in positive emotional experience (Ohm et al., 2023) yet a decrease in interpersonal warmth (Rankin et al., 2006; Sollberger et al., 2009) and empathy (Gorno-Tempini et al., 2004; Josephs et al., 2009; Landin-Romero et al., 2016; Rankin et al., 2006; Seeley et al., 2005). These seemingly paradoxical findings highlight the complex functions of the right ATL and its role in mentalizing, reward, and autonomic control (Belder et al., 2023).

In light of the above, it can be argued that the relationship between positive emotion dysregulation and the behavioral changes such as mystical and spiritual experiences may be related to the ATL. Considering case studies on patients with lateralized damage, it also seems damage to the right hemisphere plays a central role in the emergence of behavioral and emotional abnormalities such as those just described. Nevertheless, the debate regarding the lateralization (Right vs. Left hemisphere) of emotions is still unsolved, particularly within the ATLs.

The present study aimed to investigate the neural underpinning of these behavioral alterations in SD. We conducted a review of medical records targeting all behaviors that follow under the umbrella term of what we defined as "*connectedness*", unpacking it into three domains such as positivity, mysticism, and hyper-religiosity. Positivity included behaviors reflecting a dysregulation in positive emotions (Hua et al., 2018); while mysticism included spiritual encounters with supernatural entities or worlds (Cristofori et al., 2016), a distortion of time and space perception (Van Elk, 2014), and a sense of connection to a higher existence (Mohandas, 2008); hyper-religiosity includes an organized religious worship of a divine (Mohandas, 2008). Clinical observations prompted the hypothesis that people with sbvFTD are more likely to display these behaviors than people with svPPA. Our first goal was to confirm the involvement of the right ATL in feeling of connectedness and to determine how damage to this region can affect negative and positive emotional experience and behavior. Then, the second aim was to investigate the neural correlates of the three distinct behaviors to gain a deeper understanding on the underlying mechanism and networks that support the right ATL's function in emotions. Our chart review leveraged the unique variability found in the SD spectrum, providing new insights into the role of the right ATL and frontal regions in positive emotions and feelings of connection with natural and supernatural worlds.

5.2. Methods

5.2.1. Participants

The sample was an already existing dataset including 228 participants with SD (80 sbvFTD and 148 svPPA) who came to the University of California, San Francisco Memory and Aging Center for an evaluation between 1998 and 2022. The study was approved by the Committee on Human Research at the University of California, San Francisco. All participants, or their surrogates, gave their informed consent before completing the study.

All participants had an SD diagnosis using the prevailing diagnostic criteria at the time of their evaluation (Gorno-Tempini et al., 2011; Neary et al., 1998). The clinical and neuroimaging data were reassessed by a behavioral neurologist and a trained graduate student as a part of the current study to ensure that participants met current diagnostic criteria for either sbvFTD or svPPA (Gorno-Tempini et al., 2011; Younes et al., 2022). As a result, 80 sbvFTD and 148 svPPA were confirmed and constituted the final sample.

At the time of their first research visit, patients were evaluated by a multidisciplinary research team who administered a clinical interview, neurological exam, neuroimaging, and neuropsychological testing. Patients also provided a complete clinical history and provided demographic information regarding age, sex, race, ethnicity, handedness, and education. Mental status was assessed using the Mini-Mental State Examination (MMSE) with scores ranging from 0 (low cognitive function) to 30 (high cognitive function) (Folstein, Folstein, & McHugh, 1975). The Clinical Dementia Rating Scale (CDR), an informant-based measure, was used to assess functional impairment in daily life (Morris, 1993). The CDR is comprised of two scores: the CDR Total score ranges from 0 to 3, and the Sum of Boxes (CDR-Box) score ranges from 0 to 30. Higher scores on both scores indicate greater functional impairment. As part of research protocols, participants were assessed multiple times in the course of their disease but for the purpose of this chart review, we considered their first medical evaluation.

5.2.2. Neuropsychological Assessment

Participants underwent a comprehensive neuropsychological evaluation. As the research visits covered a period between 1998 and 2022, not all patients completed the same battery of neuropsychological tests. Most participants, however, completed tests that assessed visual and verbal episodic memory (e.g., word list and figure recall), executive functioning (e.g., set-shifting, working memory), language (e.g., confrontational naming), and visuospatial processing (e.g., figure copy; Kramer et al., 2003).

All participants underwent a specific evaluation of semantic knowledge, both in the verbal and nonverbal modalities. Verbal semantic knowledge was usually assessed using the modified version of the Peabody Picture Vocabulary Test (PPVT), a 16-item word-picture matching test whose scores range from 0 to 16, with lower scores indicating greater verbal semantic deficits (Dunn & Dunn, 1981; Kramer et al., 2003). Non-verbal semantic knowledge was tested by the picture version of the Pyramids and Palm Trees (PPT-P; patients matched semantically associated pictures) with scores ranging from 0 to 52 (Howard & Patterson, 1992), and lower scores indicating greater nonverbal semantic loss.

We assessed multiple domains of socioemotional functioning with a battery of task-based measures that encompassed visual face perception and affect matching by means of the two subtests of the Comprehensive Affect Testing System (CATS) (CATS Face Matching, range 0-12; CATS Affect Matching, range 0-16), where lower scores indicate greater deficits in face perception and emotional expression recognition, respectively (Froming et al., 2006).

5.2.3. Informant-based measures

Informant-based measures were also obtained to assess patients' socioemotional behavior in everyday life. We used the Interpersonal Reactivity Index (IRI) (Davis, 1983) where informants rated patients' cognitive (i.e. perspective taking) and emotional (i.e. empathic concern) empathy. Sensitivity and responsiveness to others' subtle emotional expressions were rated by informants using the Revised Self-Monitoring Scale (RSMS) (Lennox & Wolfe, 1984).

Participants also completed the Geriatric Depression Scale, a 30-item self-report questionnaire for depression with scores ranging from 0 to 30; scores above 9 indicate the presence of at least mild depressive symptoms (Yesavage et al., 1982).

5.2.3. Chart review

A retrospective chart review was conducted to evaluate connectedness. Clinical notes were assigned to three independent coders, and two coders reviewed each participant. The clinical notes included a detailed history, neurological exam, neuropsychological test scores, and imaging summary.

The goal of the clinical note review was to capture behaviors that reflected elevated connectedness. We conceptualized connectedness as including three domains that were comprised of eight specific behaviors: (1) positivity: awe, euphoria, and expansiveness; (2) mysticism: spirituality, unity, and magical thinking; (3) and hyper-religiosity: religious beliefs and religious behaviors. See **Table 1**.

For each of the eight behaviors, we used a binary coding system and assigned a 1 when the behavior was present and a 0 when the behavior was absent. These codes were mutually exclusive such that a single behavior could only be scored as 1 in one behavioral category. Each participant could, however, exhibit multiple behaviors that were scored 1 across the behavioral categories (see **Table 2** for more details). After the coders completed their independent reviews, they discussed all cases in which there was disagreement to reach a scoring consensus. After these consensus discussions, there was 100 percent agreement across all codes.

Table 1. Operationalization of positivity, mysticism, and hyper-religiosity.

Domain	Sub-domains	Definition	References
Positivity	Awe	A positive emotion that people feel when they are in the presence of something vast that they cannot immediately understand. The sources of awe are myriad and include nature, art, music, collective action (e.g., a ceremony, political march, or concert), and the courage and magnanimity of others.	Bai et al., 2017; Gordon et al., 2017; Keltner & Haidt, 2003; Shiota et al., 2006
	Euphoria	Elevated mood, jocularity, and reward-seeking symptoms.	Hua et al., 2018
	Expansiveness	Grandiose ideation reflects the belief that one has special powers, abilities, or purpose.	Sheffield et al., 2021
Mysticism	Magical thinking	A term that applied to various cognitions (e.g., astrology, paranormal beliefs, superstitions) that are inconsistent with culturally accepted laws of causality	Eckblad & Chapman, 1983; Einstein & Menzies, 2006
	Spirituality	The Inner expression of divine being which can embrace a strong connection with a strong force which can be perceived as energy, higher power, or a spiritual presence as deity or transcendent figure of consciousness.	Miller et al., 2019
	Connectedness	The feelings of unity with the world, with oneself (self-love), with others (prosocialness), and with the surrounding nature (nature connectedness).	Rahe & Jansen, 2023
Hyper-religiosity	Hyper- religious actions	Elevated organized religious worship of a divine which can include praying, reading sacral books (e.g., Bible), creating religious ornaments/places of worship.	Mohandas, 2008
	Hyper- religious beliefs	An increase and/or change in religious beliefs or in the school of religion (e.g., religious conversion).	Mohandas, 2008

Table 2. Scoring system: an example of the coding scheme for one participant.
In this example, the participant scored 2 for positivity showing both euphoria and expansiveness; 3 for mysticism encountering all its subdomains, and 1 for hyper-religiosity (HR) showing just one behavior for hyper-religiosity beliefs. The total score for connectedness was 6 out of 8 subdomains.

	Positivity			Mysticism			Hyper-religiosity	
Anecdote	Awe	Euphoria	Expansiveness	Spirituality	Connectedness	Magical Thinking	HR beliefs	HR actions
She held her hand towards a picture of Jesus and the Virgin Mary. She pointed towards Jesus, and exclaimed, "I know him!"	0	0	0	1	0	0	0	0
She developed an odd belief that mermaids were real.	0	0	0	0	0	1	0	0
She began speaking bombastically about universal ideals, such as, "justice for all." She remarked, "We need to save the people. We are all here for others."	0	0	0	0	1	0	0	0
She has always been a religious person. She became tangential, and said, "God created all religions, so they are all good	0	0	0	0	0	0	1	0
"I'm coming out more for things that I believe in… I don't care if other people don't like me… I'm only concentrating on positive things… I am who I am and I'm sorry if you can't understand me."	0	1	0	0	0	0	0	0
She has been displaying increased grandiosity. She talks about her children and grandchildren as if they have a supernatural ability to shape the future.	0	0	1	0	0	0	0	0
Total score for behavior clusters		2			3		1	

5.2.4. Neuroimaging Acquisition and Preprocessing

5.2.4.1. MRI acquisition

As a part of the research visit, patients underwent structural magnetic resonance imaging (MRI) at the UCSF Neuroscience Imaging Center. Three-dimensional T1- weighted images was obtained using either 1.5 T Tesla Siemens, 3.0 Tesla Siemens TIM Trio, or 3.0 Tesla Siemens PRISMA or 4T Tesla Siemens (Siemens Healthcare, Iselin, NJ). All structural images were acquired with a T1-weighted 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence with the following parameters: 164 coronal slices; voxel size = 1.0 x 1.0 x 1.0 mm^3; FoV = 256 x 256 mm^2; matrix size = 256 x 256; TR = 10 msec; TE = 4 msec; T1 = 300 msec; flip angle = 15° (1.5 T). For the 3T Trio and 3T Prisma, these were: 160 sagittal slices; voxel size = 1.0 x 1.0 x 1.0 mm^3; FoV

= 256 x 256 mm^2; matrix size=256 x 256; TR = 2300 msec; TE = 2.98 msec for 3T Trio and TE = 2.9 msec for 3T Prisma; flip angle = 9° (3 T).

5.2.4.2. MRI preprocessing

All T1-weighted images were first visually inspected and marked for artifacts or excessive motion by two trained research team members. During the visual inspection, a scoring system was established from 0 to 3, where lower scores indicate a bad image quality. Images marked as 0 were excluded from the sample (6.7% total – among which 3.7% sbvFTD and 3.1% svPPA). After visual inspection, the images were processed through the Computational Anatomy Toolbox (CAT12; dbm.neuro.uni-jena.de/cat, version 12.7) within Statistical Parametric Mapping (SPM12; http://www.fil.ion.ucl.ac.uk/spm/) using MATLAB 2020a (MathWorks, Natick, MA; http://www. mathworks.com).

A standard voxel-based morphometry (VBM) approach was used and included the following steps: tissue classification (gray matter (GM), white matter (WM), cerebrospinal fluid (CSF)) using unified segmentation (Ashburner & Friston, 2011), spatial normalization to a reference space using an optimized geodesic shooting procedure (according to standard protocol by Ashburner & Friston 2011) modulation by the Jacobian determinant, and spatial smoothing using a 8mm full-width at half-maximum (FWHM) Gaussian Kernel to compensate for residual variability and to permit application of random field theory for statistical inferences (according to standard protocol by Flandin & Friston, 2015).

5.2.4.3. MRI at time of the first Research Visit

We selected the T1-weighted images available within one year from the date of the first medical record. Among 228 patients (80 sbvFTD, 148 svPPA), 63 sbvFTD (27.6%) and 100 svPPA (43%) had a T1 scan available within a year of the first research visit. Following visual inspection, the final sample included 57 of sbvFTD and 95 scans of svPPA patients.

5.2.4.4. Individual atrophy (W-Score) Maps

To create participant-specific maps of atrophy, the smoothed gray matter images underwent transformation into W-score maps as described previously (Iaccarino et al., 2021; Ossenkoppele et al., 2015). W-score maps are voxelwise statistical maps that indicate the degree to which voxelwise brain tissue volumes in each patient deviate from those in neurologically intact controls considering the influence of relevant covariates. For this study, the W-score model was developed by computing a voxelwise multiple regression model for the pre-processed imaging data for a sample of 205 neurologically intact controls (mean age 69 SD= 8.9; range 48-88; 126 females) including age at the MR scans, sex, scanner type, and total intracranial volume were included as covariates. We estimated their effect on the voxel-specific value of a segmented gray matter tissue density map in the control sample Ossenkoppele et al. (2015). The voxelwise beta coefficients from the regression in neurologically intact controls were than applied to the pre-processed imaging data from each patient to derive covariate-adjusted brain tissue volumes (i.e., W-scores) with the following formula: *(observed brain tissue volume − expected brain tissue volume)/standard deviation* of the residuals for that voxel in neurologically intact controls. Since the distribution of W-scores is analogous to that of Z-scores, the W-map for each patient was binarized using an uncorrected voxel-level threshold of p<0.05 one-tailed (i.e., W-score <-1.64, as in Iaccarino et al., 2021) and cluster extent threshold of a least 100 contiguous voxels, yielding a binary map of the presence or absence of atrophy at each voxel across the brain.

5.2.5. Statistical Analyses

5.2.5.1. Demographic, Clinical and Cognitive Status at Time of the first Clinical Visit

Demographics, clinical, and cognitive variables were compared between the sbvFTD and svPPA groups. Mann-Whitney t-tests were performed for nonparametric measures, chi-square tests were used to assess the group differences in sex and handedness, and Fischer's exact tests for race/ethnicity. Analyses were conducted using R through *JAMOVI* (version 2.3) and R studio (version 2023).

5.2.5.2. Positivity, Mysticism, and Hyper-religiosity in SD

We computed a total connectedness score by summing the scores across the behavioral domains (scores ranged from 0-8). For each of the behavioral domains, we computed total scores for positivity (scores ranged from 0-3), mysticism (scores ranged from 0-3), and hyper-religiosity (scores ranged from 0-2) by summing the codes in each category. We used chi-square tests of independence to compare the frequency of total connectedness as well as total positivity, mysticism, and hyper-religiosity between the sbvFTD and svPPA groups. Chi-square test was also performed to assess whether there were group differences at the level of individual behaviors (spirituality, magical thinking, connectedness, awe, euphoria, expansiveness, religiosity beliefs and actions).

We next analyzed the correlation between the total connectedness scores (total number of subdomains displayed by each participant) and informant-based measures of socioemotional behavior, such as the cognitive empathy (IRI- perspective taking) and the emotional empathy (IRI-empathic concern). The correlation analyses used a Pearson's r Coefficient.

5.2.5.3. Anterior Temporal Lobe Asymmetry at the First Clinical Visit

Using the MRI scan at the first clinical visit from each participant, we first validated that the svPPA and sbvFTD groups exhibited the anticipated pattern of lateralized atrophy in the anterior temporal lobe at the time of diagnosis. We computed an anterior temporal lobe laterality index through previously established procedures (Borghesani et al., 2020). In brief, we extracted average gray matter volume from the specified left and right anterior temporal lobe regions of interest, utilizing the combined subregions derived from regions of interest based on previous findings of dissociable functional and structural connectivity profiles (Papinutto et al., 2016; Pascual et al., 2015). The GM volumes were then normalized based on the total GM volume in the entire sample and then adjusted by the average total GM volume of the healthy controls in our sample to consider the deviation from expected values. Asymmetry scores for the left and right anterior temporal lobes were determined using the formula: (left – right) / (left + right). Negative values indicated a more pronounced left-lateralized (i.e., left greater than right) atrophy in the anterior temporal lobe, while positive values indicated right-lateralized (i.e., right greater than left) anterior temporal lobe atrophy.

5.2.5.4. Voxel-based morphometry across SD

First, we conducted a whole-brain voxel-based morphometry analysis using SPM12 on W-score maps to compare the two SD groups (sbvFTD and svPPA) using a two-sample t-test. Significant clusters were identified across the whole brain using a *T*-score threshold corresponding to $p<.05$ familywise error (FWE) corrected. Next, we performed four general linear models on the W-score maps in SPM12 to determine the neural correlates of total connectedness as well as total positivity, total mysticism, and total hyper-religiosity (controlling for total GM volume).

5.3. Results

5.3.1. Demographic, Clinical, and Cognitive Status at Time of the First Clinical Visit

Results for demographic, clinical, and cognitive status are collected in **Table 3**.

Participants with SD were on average 74.4 years of age, 112 males and 116 females, mostly White American (87.9%) and right-handed (85%) and had on average 15.9 years of education. Overall, the CDR-Box was on average 4.84 (3.35) and a MMSE of 21 (8.06).

Participants with sbvFTD were 35 males and 45 females, on average 73.4 years of age, mostly White American (86.1%), 83% of them were right-handed and had on average 15.9 years of education. Participants with svPPA were 77 males and 71 females, on average 74.9 years of age, mostly White American (88.5%), 90.3% of them were right-handed and had on average 15.9 years of education. When compared, the two groups did not differ in their demographic profile for each of the variables reported (ps > .05), despite the sbvFTD group had a higher disease severity than the svPPA group when considering the CDR-Box, [$F(1, 171) = 3.87$, $p = 0.051$] and a worse global cognitive status (MMSE) [$F(1, 197) = 5.5$, $p = 0.02$]. No difference was found for CDR Total Scores ($p > .05$).

When assessed for differences in their cognitive abilities, the svPPA group showed lower scores than sbvFTD on verbal memory CVLT 30' (short delay) [$F(1, 163) = 18.59$, $p < .001$] and CVLT 10' (long delay) [$F(1, 163) = 11.63$, $p < .001$], semantic fluency (animal fluency) [$F(1, 171) = 20.6$, $p < .001$], confrontational naming (Boston Naming Test total correct) [$F(1, 180) = 22.97$, $p < .001$]; repetition [$F(1, 155) = 7.68$, $p = .06$], and verbal semantic knowledge (PPVT) [$F(1, 221) = 19.81$, $p < .001$].

Instead, the sbvFTD group showed lower scores than svPPA on visual memory (Benson Figure-delay) [$F(1, 184) = 4.11$, $p = .044$], affect matching (CATS Affect Matching) [$F(1, 115) = 11.71$, $p < .001$], empathetic concern (IRI- Empathic Concern) [$F(1, 147) = 18.06$, $p <.001$] and perspective taking (IRI-Perspective Taking) [$F(1, 147) = 10.33$, $p = .002$], and depression (GDS) [$F(1, 115) = 4.58$, $p = .034$].

No group differences were detected for any of the other cognitive variables.

Table 3. Demographics, cognitive, and clinical information by diagnostic group.
Means and standard deviation are indicated. Statistical differences among the two groups are reported on the right, the ones significant highlighted with *.

a. Epidemiology and functional scales

	SD (*n*=228)	**svPPA (*n*=148)**	**sbvFTD (*n*=80)**	***Significant Differences***
Age	74.4 (8.96)	74.9 (9.07)	73.4 (8.75)	p=.252
Gender (Males; Females)	112M; 116F	77M; 71 F	35M; 45 F	p=.233
Handedness (%Right; % No-Right)	85% 12% NR	90.% R; 9.7 NR	83% R; 17% NR	p=.121
Years of education	15.9 (3.21)	15.9 (3.27)	15.9 (3.1)	p=.995
CDR score, max=3	0.9 (0.59)	0.87 (0.6)	0.94 (0.58)	p=.442
CDR Box Score, max=18	4.84 (3.35)	4.47 (3.39)	5.5 (3.21)	p=.051*
Global cognition				
MMSE, max=30	21 (8.06)	20 (8.38)	22.7 (7.25)	p=.02*

b. Cognitive status

	SD (*n*=228)	svPPA (*n*=148)	sbvFTD (*n*=80)	*Significant Differences*
Visuospatial processing				
Benson Complex Figure-copy, max=17	15.2 (2.01)	15.4 (1.91)	15 (2.16)	p=.237
VOSP Number Location max=10	8.89 (1.65)	8.92 (1.67)	8.86 (1.62)	p=.827
Verbal and visual Episodic memory				
CVLT 30' short delay free recall, max=9	2.95 (2.62)	2.29 (2.38)	4.02 (2.66)	p<.001*
CVLT 10' long delay free recall, max=9	1.75 (2.33)	1.27 (1.95)	2.51 (2.68)	p<.001*
Benson Complex Figure-delay, max=17	6.08 (4.72)	6.62 (4.84)	5.19 (4.39)	p=.044*
Executive functioning				
Digit Span- backward	4.47 (1.48)	4.31 (1.48)	4.72 (1.46)	p=.067
Trails (correct*minutes)	18.8 (14.4)	18.8 (13.6)	18.7 (15.8)	p=.964
Language and object semantics				
Verbal Agility, max=5	5 (1.46)	4.92 (1.63)	5.15 (1.08)	p=.355
Repetition, max=5	3.41 (1.45)	3.16 (1.53)	3.81 (1.22)	p=.006*
WRAT Total	51.9 (13.1)	50.6 (12.5)	54.2 (14)	p=.165
Lexical fluency- n	7.85 (4.79)	7.3 (4.72)	8.74 (4.72)	p=.057
BNT, max=15	5.31 (4.21)	4.2 (3.49)	7.12 (4.67)	p<.001*
Semantic fluency- n	8.32 (5.62)	6.9 (5.08)	10.7 (5.71)	p<.001*
PPVT, max=16	6.4 (5.68)	5.23 (5.38)	8.66 (5.59)	p<.001*
Pyramids and Palm Tree Pictures, (max %=)	85 (15)	90 (8)	84 (39)	p=.486
Face perception				
CATS Face Matching, max=12	11.4 (1.37)	11.5 (1.62)	11.3 (0.88)	p=.584
Social function and emotion				
CATS Affect Matching, max=16	10.6 (2.98)	11.4 (2.2)	9.59 (3.52)	p<.001*
Informant-based measures				
IRI-Empathetic Concern, max=24	21.7 (8.59)	23.9 (6.85)	18 (10)	p<.001*
IRI-Perspective Taking, max=24	14.9 (7.62)	16.4 (7.36)	12.3 (7.44)	p=.002*
Self-Monitoring RSMS, max=65	29 (14.6)	29.4 (13.8)	28.5 (16)	p=.757
Geriatric Depression GDS, max=30	2.69 (4.75)	1.88 (3.88)	3.75 (5.54)	p=.034*

5.3.2. Positivity, Mysticism, and Hyper-religiosity were Common in Semantic Dementia, especially in sbvFTD

Across the full SD sample, 61.8% of people exhibited at least one of the eight coded behaviors. Overall, positivity was the most common behavioral domain displayed across the sample (55.3%), followed by hyper-religiosity (13.1%), and then mysticism (12.3%) (see Figure 1). For examples of behaviors that were captured in each domain, see the **Appendix B**. When comparing the two clinical groups, sbvFTD patients showed higher rates of positivity (75% of sbvFTD patients vs 44.6% svPPA; χ^2 = 19.4, p < .001); mysticism (21.3% of sbvFTD patients vs 7.4% svPPA patients, χ^2 = 9.2, p = 0.002; and hyper-religiosity (25% of sbvFTD patients vs 6.8% of svPPA patients, χ^2 =15.1, p<.001) than svPPA (see Figure 1 and Table 4).

Figure 1. Frequencies of occurrence of total connectedness as well as positivity, mysticism, and hyper-religiosity across sbvFTD and svPPA. Comparisons statistically significant are highlighted with *).

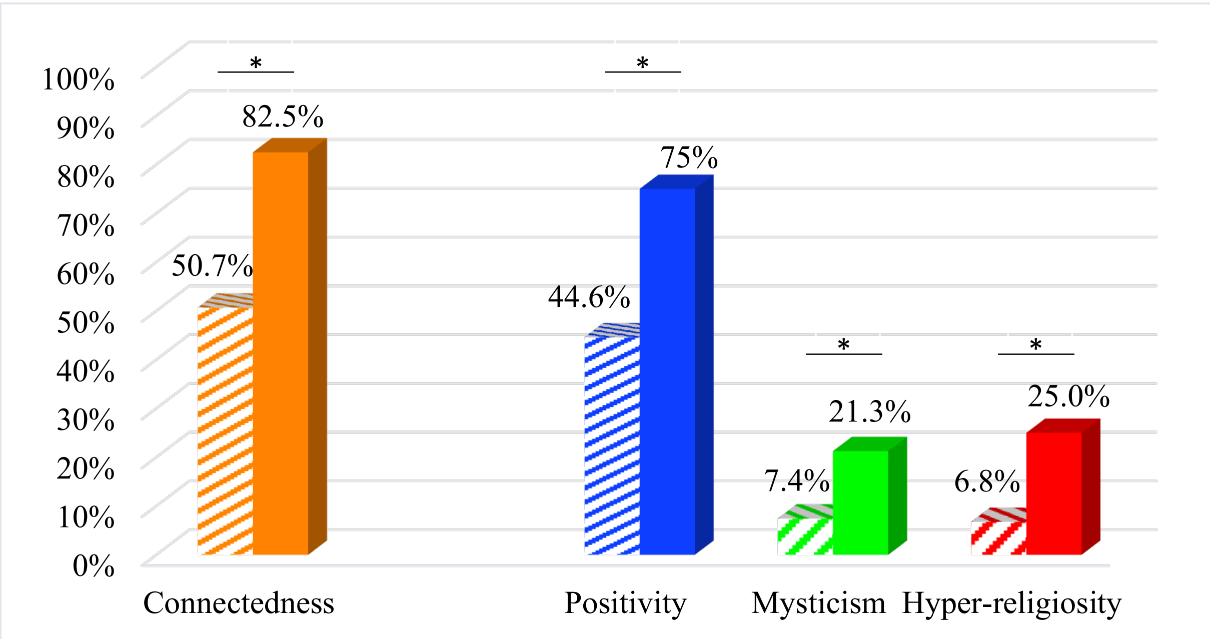


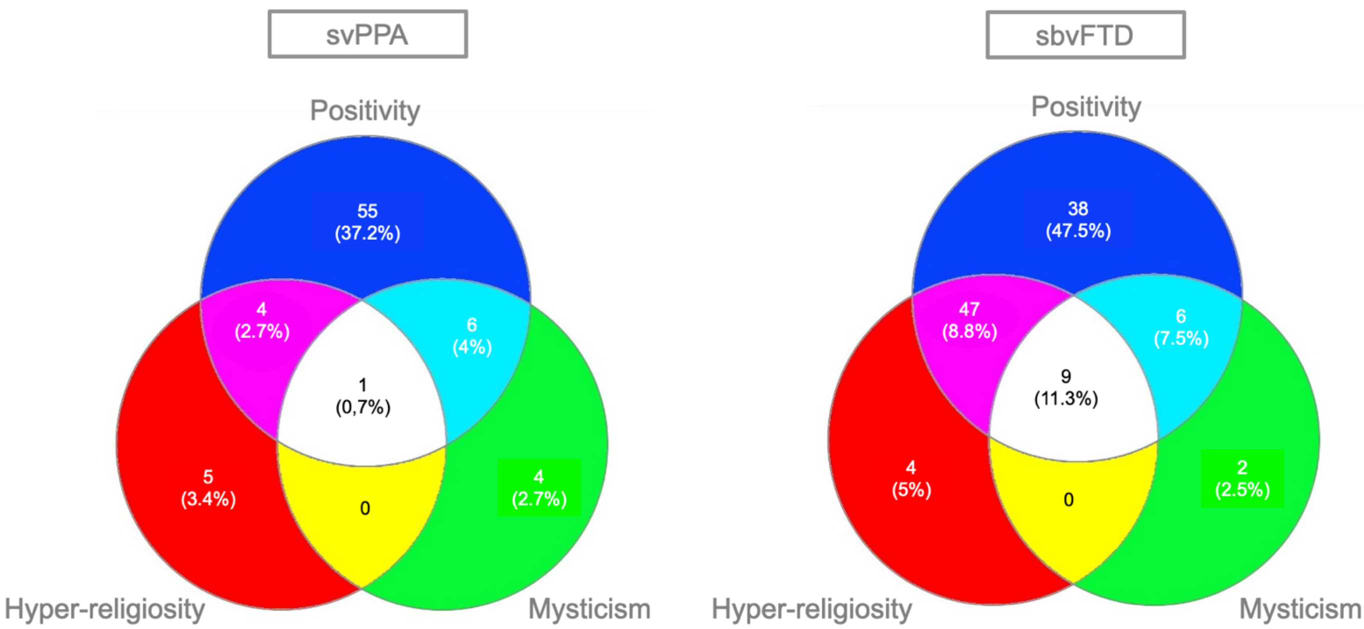
Table 4. Group comparison (sbvFTD vs svPPA) on the frequencies of occurrence of the three target behaviors and their subdomains using a Chi-square test (present vs no present).

	SD (n=228)	svPPA (n=148)	sbvFTD (n=80)	Stats	p value
Global Score (0-8) % (mean, SD)	61.8% (0.98, 1.1)	50.7% (0.68, 0.78)	82.5% (1.53, 1.39)	$\chi^2 = 22.3$	$p < .001$
Mysticism Score (0-3) % (mean, SD)	12.3% (0.16, 0.49)	7.4% (0.07, 0.26)	21.3% (0.33, 0.73)	$\chi^2 = 9.2$	$p = .002$
Spirituality % (mean, SD)	5.7% (0.06, 0.23)	1.4% (0.01, 0.12)	13.8% (0.14, 0.35)	$\chi^2 = 14.8$	$p < .001$
Unity % (mean, SD)	8.3% (0.08, 0.28)	6.1% (0.06, 0.24)	12.5% (0.13, 0.33)	$\chi^2 = 2.8$	$p = .094$
Magical Thinking % (mean, SD)	2.2% (0.02, 0.15)	0	6.3% (0.06, 0.24)	$\chi^2 = 9.46$	$p = .002$
Positivity Score (0-3) % (mean, SD)	55.3% (0.66, 0.67)	44.6% (0.52, 0.63)	75% (0.91, 0.66)	$\chi^2 = 19.4$	$p < .001$
Awe % (mean, SD)	1.3% (0.01, 0.11)	0	1.3% (0.04, 0.19)	$\chi^2 = 5.62$	$p = .018$
Euphoria % (mean, SD)	48.2% (0.48, 0.5)	26.8% (0.41, 0.49)	21.5% (0.61, 0.49)	$\chi^2 = 8.35$	$p = .004$
Expansiveness % (mean, SD)	16.2% (0.16,0.37)	7% (0.11, 0.31)	9.2% (0.26, 0.44)	$\chi^2 = 9.11$	$p = .03$
Hyper-religiosity Score (0-2) % (mean, SD)	13.2% (0.16,0.43)	6.8% (0.09, 0.35)	25% (0.29, 0.53)	$\chi^2 = 15.1$	$p < .001$
Beliefs % (mean, SD)	6.1% (0.06,0.24)	6.1% (0.06, 0.24)	6.3% (0.06, 0.24)	$\chi^2 = 0.003$	$p = .96$
Actions % (mean, SD)	9.6% (0.1, 0.3)	2.7% (0.03, 0.16)	22.5% (0.23, 0.42)	$\chi^2 = 23.3$	$p < .001$

We then analyzed the behaviors in each domain separately. Within the domain of positivity, sbvFTD showed the highest rates of awe (3.8% of sbvFTD vs no svPPA, $\chi^2 = 5.62$, $p = .018$); euphoria (61.3% of sbvFTD vs 41.2% of svPPA, $\chi^2 = 8.35$, $p = .004$); expansiveness (26.3% of sbvFTD vs 10.8% svPPA, $\chi^2 = 9.11$, $p = .003$). Within the domain of mysticism, sbvFTD showed the highest rates of spirituality (13.8% of sbvFTD vs 1.4% of svPPA, $\chi^2 = 14.8$, $p < .001$); magical thinking (6.3% of sbvFTD vs no svPPA, $\chi^2 = 9.46$, $p = .002$); and hyper-religious behaviors (22.5% of sbvFTD vs 9.6% of svPPA, $\chi^2 = 23.3$, $p < .001$). Although not significantly different, sbvFTD showed a trend for more frequent experiences of unity (12.5% of sbvFTD vs 6.1% of svPPA, $\chi^2 = 2.8$, $p = .094$). No significant difference was reported for hyper-religious beliefs, $\chi^2 = .003$, $p = .096$ (see Table 4).

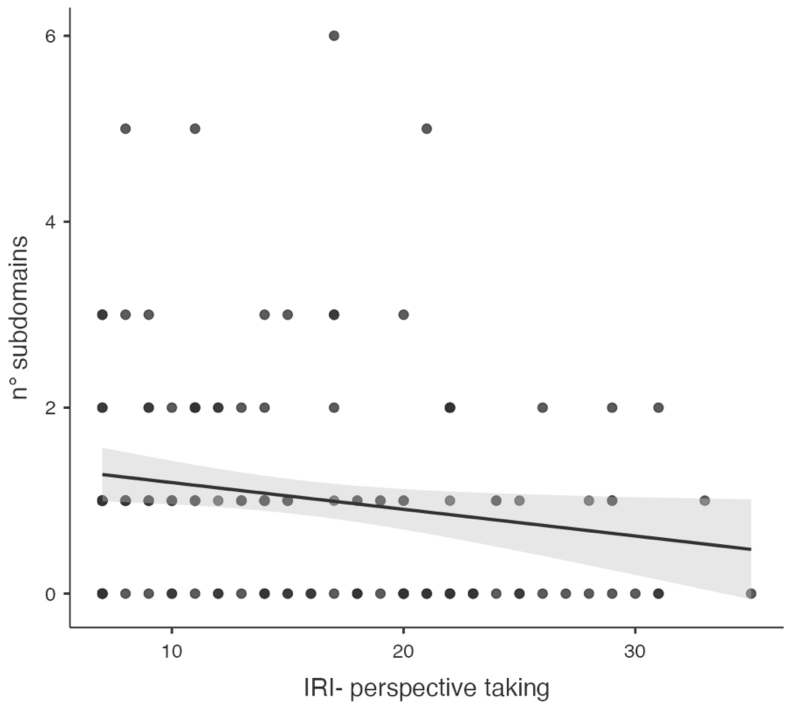
Compared to the svPPA group more people in the sbvFTD group showed elevations in any one of the behavioral domains. Furthermore, 16.3% of people with sbvFTD showed statistically significant changes in two out of three of the behavioral domains compared to people with svPPA (6.8%), and 11.3% of people with sbvFTD showed statistically significant changes in all the three behavioral domains compared to people with svPPA (0.7%) [$\chi^2 = 33.2$, $p < .001$]. The co-occurrence of the three behavioral domains in the two groups is represented by the Venn diagrams in Figure 2.

Figure 2. The Venn diagrams show the co-occurrence between the three cluster of behavioral domains within each diagnostic group. Participants showing both positivity and mysticism are in light blue; the ones showing positivity and hyper-religiosity are in pink; the ones showing all the three domains are in white. None showed both mysticism and hyper-religiosity (yellow).



Lastly, the correlation analyses between the number of subdomains encountered by each participant and the two subscales of the IRI questionnaire showed a negative correlation with the perspective taking [Pearson's rho = -.181, p = .03] but not the empathic concern [Pearson's rho = -.02, p = .789] subscale (Figure 3).

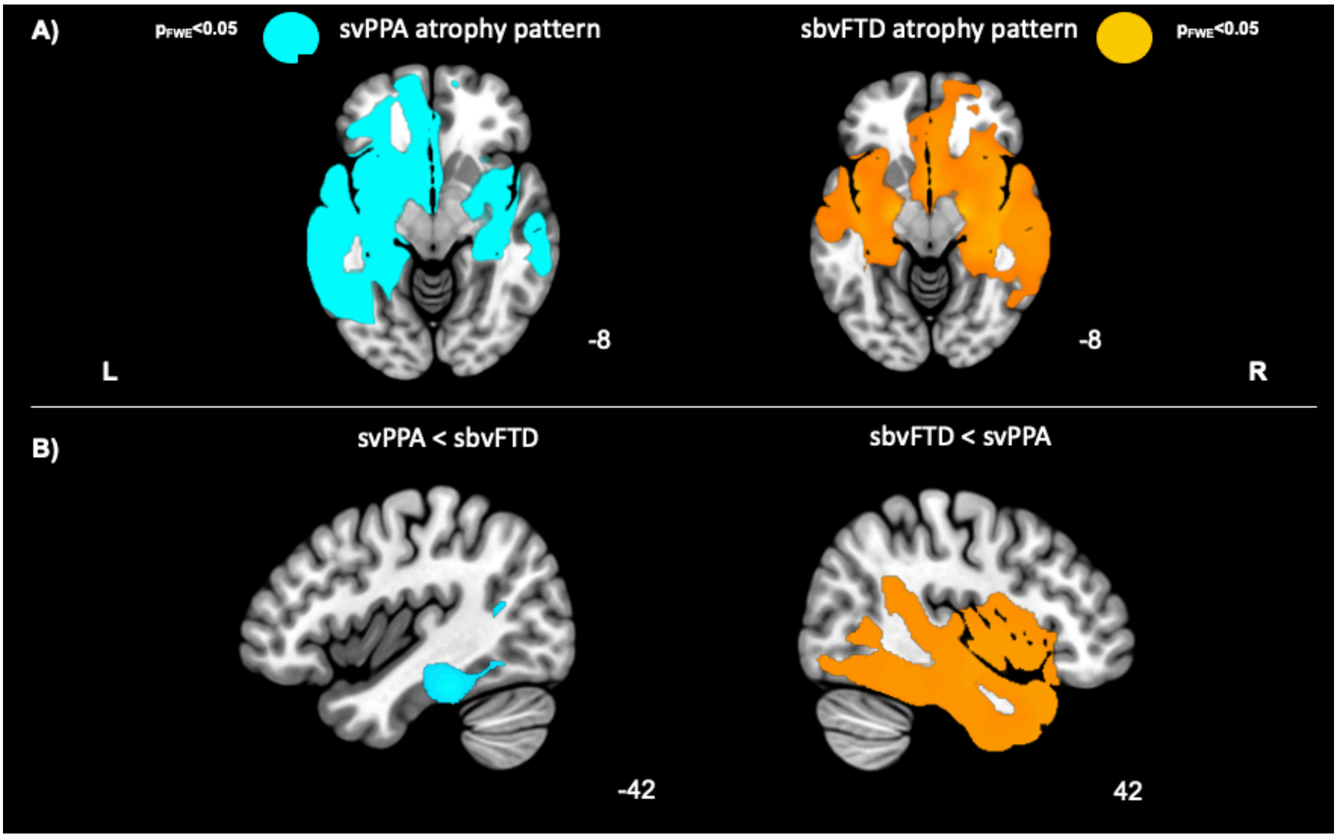
Figure 3. The feeling of connectedness is negatively correlated with the ability to consider other's perspective. The graph shows the significant correlation between the number of subdomains encountered and the perspective taking subscale of the IRI questionnaire.



5.3.3. Positivity, Mysticism, and Hyper-religiosity in SD Relate to Right ATL Atrophy

At the time of the first medical record, participants in the svPPA group had smaller gray matter volume in left inferior temporal gyrus, left middle temporal gyrus, left superior temporal gyrus ($p_{FWE} < .05$), and participants in the sbvFTD group had smaller gray matter volume in the right superior frontal gyrus and right temporal pole ($p_{FWE} < .05$) (Figure 3).

Figure 3. Distinct atrophy patterns in svPPA and sbvFTD. Whole-brain voxel-based morphometry analyses performed on W-score maps (controlling for GM) confirmed that the svPPA group has smaller gray matter volume in the left temporal pole than the sbvFTD group; on the contrary the sbvFTD group had smaller gray matter volume in the right temporal pole than the svPPA group ($p_{FWE} < .05$). Statistical maps are superimposed on the Montreal Neurological Institute template.



A linear regression analysis revealed that higher connectedness in SD related to smaller gray matter volume in the right ATL (Figure 4.A and Table 5). In separate regressions of each behavioral domain, higher positivity related to smaller gray matter volume in the right ATL, right insula, right orbitofrontal cortex, right angular gyrus, right precentral gyrus, right cingulate cortex, and right fusiform gyrus. Greater experiences of mysticism were associated with smaller gray matter volume in the right precentral gyrus, right medial superior frontal gyrus, right fusiform gyrus, right ATL, right orbitofrontal cortex, and right superior temporal gyrus. Hyper-religiosity was associated with smaller gray matter volume in the right ATL, right superior frontal gyrus, right superior temporal gyrus, right fusiform gyrus, right angular gyrus, and right orbitofrontal cortex. See Figure 4.B and Table 5 for the distinct neural correlates for each domain.

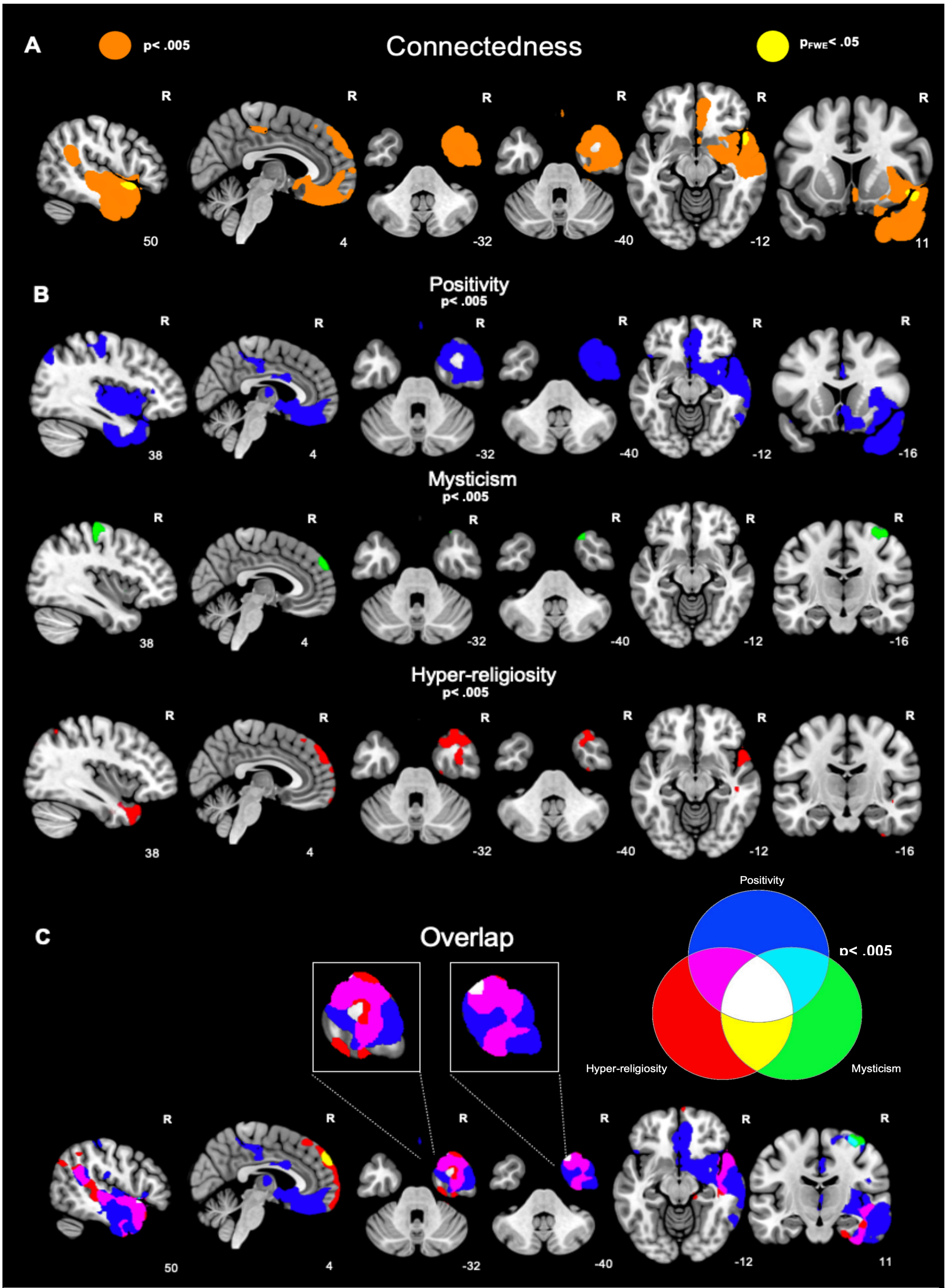
Across the regression analyses, all the behaviors had overlapping correlates in the right fusiform gyrus, right superior and middle temporal gyrus. While positivity and mysticism both related to smaller gray matter volume in the right precentral and post-central gyri, positivity and hyper-religiosity related to smaller gray matter volume in the right temporal lobe, right angular gyrus, right supramarginal gyrus and right insula. Mysticism and hyper-religiosity both correlated with smaller gray matter volume in the right medial superior frontal lobe (Figure 4.C).

Table 5. Neural correlates of total connectedness as well as positivity, mysticism, hyper-religiosity.

Anatomical region	**Cluster volume (mm^3)**	**MNI coordinates** x	y	z	Maximum T-score	*Peak level* ***p*- value**
Connectedness						
Right Anterior Temporal Lobe	277	50	15	-9	5.31	.013*
Positivity						
Right Anterior Temporal Lobe	14166	48	9	-10	4.67	<.001
Right Insula	14166	34	-22	0	4.49	<.001
Right Orbitofrontal Cortex	1945	2	46	-30	4.2	<.001
Right Angular Gyrus	727	51	-46	27	4.16	<.001
Right Precentral Gyrus	565	28	-22	52	4.06	<.001
Right Cingulate Cortex	380	3	-21	46	3.69	<.001
Right Fusiform Gyrus	12	27	15	-41	3.16	.001
Mysticism						
Right Precentral Gyrus	355	27	-21	51	4.11	<.001
Right Medial Superior Frontal Gyrus	233	2	60	38	3.89	<.001
Right Fusiform Gyrus	61	25	13	-46	3.56	<.001
Right Anterior Temporal Lobe	61	27	16	-50	3.56	<.001
Right Orbitofrontal Cortex	23	58	15	-4	3.42	<.001
Right Superior Temporal Gyrus	23	50	13	-7	3.42	<.001
Hyper-religiosity						
Right Anterior Temporal Lobe	2177	54	18	-30	3.87	<.001
Right Superior Frontal Gyrus	1116	8	56	40	5.01	<.001*
Right Superior Temporal Gyrus	788	70	-46	14	4.46	<.001
Right Fusiform Gyrus	232	27	-30	27	3.6	<.001
Right Angular Gyrus	163	40	-60	56	3.87	<.001
Right Orbitofrontal Cortex	17	58	21	2	3.3	<.001

Voxel-based morphometry analyses (controlling for gray matter) revealed that smaller gray matter volume in Right Anterior Temporal Lobe was associated with elevated connectedness. Montreal Neurological Institute coordinates (x, y, z) are reported for maximum T-score in each cluster. All results are significant at p < .001 uncorrected. *=Results significant at p_{FWE} < .05. Cluster smaller than 15 mm^3 were excluded.

Figure 4. Neural correlates of Connectedness. A) The occurrence of the three domains in right anterior temporal lobe. B) Distinct neural correlates of positivity, mysticism, and hyper-religiosity. C) The overlap of three behavioral domains.



Whole-brain voxel-based morphometry on W-score maps (controlling for GM) showed: the co-occurrence (white) of all three domains in the right superior temporal lobe and right fusiform gyrus (slices -32; -40); the co-occurrence of positivity and mysticism (light blue) in the right precentral (slice 11); the co-occurrence of positivity and hyper-religiosity (pink) in the right temporal lobe and right angular gyrus (slices 50; -32; -40; -12; 11); the co-occurrence of mysticism and hyper-religiosity (yellow) in the right superior frontal lobe (slice 4). The legend displays the domains by the colored circles and their overlaps. Statistical maps are superimposed on the Montreal Neurological Institute template.

5.4. Discussion

Our results indicate that elevated experiences of connectedness are common in SD. When breaking this construct apart into its component domains, more than half of the participants with SD displayed heightened positivity. A smaller subset of the sample exhibited heightened mysticism and hyper-religiosity. Among people with SD, those with sbvFTD had higher rates of these behaviors than those with svPPA. Heightened feelings of awe, euphoria, and expansiveness as well as increases in spirituality, magical thinking, and hyper-religious behaviors were more common in sbvFTD than svPPA. Although not statistically significant, unity and hyper-religious beliefs also trended toward enhancement in that group. The neuroimaging analyses confirmed that individuals across the SD spectrum who exhibited greater feelings of connectedness had smaller gray matter volume in the right ATL. While elevations in each of the behavioral domains related to smaller volume in the right ATL, each also had distinct neural correlates that were all located in the right hemisphere. Greater positivity related to smaller gray matter volume in the right orbitofrontal cortex, angular gyrus, and precentral gyrus; greater mysticism related to smaller volume in the right precentral gyrus, medial superior frontal gyrus; and hyper-religiosity related to smaller volume in the right superior frontal gyrus, angular gyrus, and inferior temporal gyrus.

All the domains had overlapping neural correlates in the right fusiform gyrus, right superior and middle temporal gyrus. The presence of positivity and mysticism within the same patients was associated to reduced gray matter volume in the right precentral and postcentral gyri, while positivity and hyper-religiosity were both linked to smaller gray matter volume in the right temporal lobe, as well as the right angular gyrus, right supramarginal gyrus and right insula. Additionally, mysticism and hyper-religiosity correlated with smaller gray matter volume in the right medial superior frontal lobe.

Prior case studies have noted that people with SD may have increased feelings of connectedness with their senses and with the natural and supernatural words (Block & Miller, 2019). Our results are consistent with this and showed most people with SD had heightened feelings of connectedness. As feelings of connectedness are multifaceted, we next broke this construct down into its component domains of positivity, mysticism, and hyper-religiosity. There have also been case report descriptions of elevated feelings of positivity in SD (Block & Miller, 2019; Edwards-Lee, 1997; Ohm et al., 2023; Shdo et al., 2022; Sturm et al., 2015). In the present study, most participants with SD displayed heightened positivity, and fewer showed elevations in mysticism and hyper-religiosity. Differences between sbvFTD and svPPA have also been reported in individual cases such that experiences of connectedness with spiritual overtones may be more prevalent in people with right-lateralized atrophy (Block & Miller, 2019; Ohm et al., 2023). The present study confirmed that elevated feelings of connectedness in SD were greater in sbvFTD than svPPA. Compared to the svPPA group, the sbvFTD group had higher rates of positivity, mysticism, and hyper-religiosity than the svPPA group.

The neuroimaging analyses showed elevated feelings of connectedness were associated with smaller gray matter volume in the right ATL. As the central hub for the semantic appraisal network, the right ATL may play a crucial role in the hedonic tuning of socioemotional knowledge, making it a potential substrate in the emergence of all these experiences (Olson et al., 2007). At the level of the individual behavioral domains, some differences emerged in their neural correlates. While there was overlap among the domains in the superior and middle temporal pole and in the right fusiform gyrus, there were also distinctions. Whereas positivity related to the right cingulate cortex and the left superior temporal gyrus, hyper-religiosity related to right parietal gyrus. Mysticism does not have distinct neural correlates. While right hemisphere damage in FTD disrupts negative emotion recognition, production, and regulation (Irish et al., 2013; Rosen, 2002), in our prior research we have found increased positive emotional reactivity (i.e., smiling and laughing behaviors) is linked to damage in emotion regulation systems in the left hemisphere (specifically the left superior temporal gyrus). As a result, this may cause a 'release' of emotion generator systems in the left hemisphere (Shdo et al., 2022; Sturm et al., 2015). Whether elevated positivity in sbvFTD relates to loss in the right ATL as negative emotions recede or to gain in positive emotions due to release in the left hemisphere emotion generators is a question for future studies.

In the present study, we found elevated mysticism and hyper-religiosity also related to right ATL atrophy. Atrophy in the dorsal medial stream was associated with elevations in both mysticism and hyper-religiosity. This includes both the right superior temporal lobe, as well as the right medial superior frontal lobe, which is part of the prefrontal cortex. It is possible that frontal and temporal regions play a homeostatic function in these experiences and a down-regulation of frontal inhibitory processes in the dorsal prefrontal cortex could play a role in these behaviors. Moreover, a more pronounced disruption in the dorsal stream may result in greater dependence on the ventral stream. According to the ventral-dorsal gradient (Bonner & Price, 2013; Mesulam, 2023; Tyler et al., 2004), the ventral structures are more involved in the processing of concrete information, such as object concepts, whereas the dorsal structures on abstract knowledge of social concepts. This could explain why people with SD experienced a feeling of connection to non-living entities rather than human beings, potentially contributing to their lack of compassion towards others.

One potential limitation of this study is that it relies on a qualitative review of medical records. This could imply that our results may be influenced by the neurologists' impressions, the judges' interpretation of the charts and scoring system used. To address this limitation, it will be crucial to utilize a standardized tool during the clinical interview to gather information from both the caregiver and patient regarding a set of standardized questions that evaluate these peculiar changes in behaviors. This approach can assist the neurologist in conducting a more accurate clinical assessment leading to the differential diagnosis. Furthermore, structural voxel-based morphometry does not allow us to draw any conclusions regarding the functional connectivity between the right ATL and the other brain regions. Despite lesions studies have shown the right temporal involvement in mystical and spiritual experiences (Brooks & Hoblyn, 2005; Cristofori et al., 2016; Joseph, 2001; Saver & Rabin, 1997), the temporal lobe is not the sole determinant. The ATL is connected to the prefrontal regions, which are key areas of default mode network and are responsible for socioemotional interactions, as well as in perspective-taking (Block & Miller, 2019; Olson et al., 2007). A future line of research can explore the functional connectivity among the two hemispheres to clarify the hemispheric involvement in processing emotions and valence.

To conclude, our chart review contributes to the field by enhancing our understanding of the nature of these emotional and behavioral alterations observed in patients with SD.

Relatively little is known about social and emotional alterations in SD. Previous research has linked right ATL atrophy in FTD to behavioral changes such as lack of empathy (Rankin, 2020; Rankin et al., 2006), disinhibition (Liu et al., 2004), and socially inappropriate behaviors (Vonk et al., 2020). FTD patients with right ATL involvement also demonstrate greater impairments in social concepts than animal concepts (Zahn et al., 2009) and have trouble recognizing (Perry et al., 2001; Vonk et al., 2020) and expressing (Pressman et al., 2023) emotions. To our knowledge, however, this study was the first to report the emergence of elevated feelings of connectedness in a large cohort of patients with SD that was clinically and anatomically characterized. Leveraging the variety of phenotypes in SD, we gained insights into the nature of the feeling of connectedness and provided helped to elucidate its neural underpinnings.

GENERAL DISCUSSION

The main aim of this thesis was to investigate the semantics of emotions, exploring the affective and psycholinguistic factors that influence how people store emotions by examining their temporal and spatial correlates in the brain. My studies confirmed the representation of emotional concepts as nodes within an associative network in the semantic memory. The semantics of emotions represents a multifaceted space where categories of emotions lack clear boundaries, instead unfolding within a gradient of combined experiences and manifestations (Cowen et al., 2019; Cowen & Keltner, 2021). This expands upon the traditional circumplex model, which organizes emotion concepts along the two-dimensional axes of valence and arousal (Russell, 1980), by considering the semantic similarity within the same emotion category (e.g., irritation and anger are closely related concepts within the anger category). In this model, each emotion concept is represented by a word used to describe it (herein the semantic valence, or socioemotional knowledge), as well as the feeling attached to that word related to all autonomic and sensory responses (herein the affective valence). By applying different behavioral and neuroimaging techniques, I was able to disentangle the temporal and anatomical course of affective and semantic valence in the brain.

Studies 1 and 2, as a part of the same research project, used an affective priming paradigm to explore the role of valence and semantics during the automatic elaboration of emotional words. Results suggest that negative and positive information may be processed differently in the brain, a concept already discussed in the literature. These studies shed light on the importance of parsing the fine-grained semantic differences within the negative domain. By using pain as a model, I detected a significant interaction between the valence and semantics of the stimuli, which generates a unique facilitatory response to pain. These results were also reflected in my analysis of event-related potentials on EEG activity associated with this phenomenon. The ERP analysis provides evidence of the time course of the processing of affective and semantic valence, highlighting that individuals automatically encode the semantics of the stimulus first, and only at a late stage of stimulus elaboration, they perform an affective evaluation. According to these studies, in automatic stimulus processing, the evolutionary role of the valence of a negative stimulus depends on the granularity of semantic concepts within the negative domains generating specific responses for each type of content.

Study 3 confirmed the issue by applying an emotion fluency task that relies on voluntary mechanisms. My results showed a tendency towards a negativity bias, which emphasizes the need for further consideration of the detailed nature of semantic concepts within the negative domains. This allows individuals to recall more negative words than positive ones. Contrary to my predictions, the valence was not a predictor of the order in which participants recall the words in the fluency task.

Instead, semantic relatedness played a pivotal role in driving performance on the task. It is likely that even at a voluntary stimulus processing, the semantic valence had priority over the affective valence in shaping the structure of emotion in the brain. So far, the implications of my studies prompt the study of the brain correlates for affective and semantic valence.

Hence, Study 4 used patients with semantic dementia as a model to study the neural correlates of affective and semantic valence. The asymmetric atrophy of the anterior temporal pole in the two variants of semantic dementia, namely svPPA and sbvFTD, results in different semantic deficits together with changes in behaviors and emotions. The varied pattern of deficits observed in the two groups clearly delineates the distinction between semantic knowledge for objects and emotions. My findings suggest that atrophy in the right temporal and frontal regions results in changes in behavior and emotions characterized by a feeling of connectedness and over-positivity. I can speculate that the patients with more right-sided atrophy, as sbvFTD, have lost the semantic knowledge for negative emotions leading to an increase in positive emotions. This means that they may potentially have lost the associated feeling attached to the word of a negative concept, what I have previously called affective valence, making it difficult for them to comprehend and express that emotion. The study of patients with semantic dementia provides a meaningful tool to assess the neural correlates of socioemotional semantics with the right anterior temporal lobe playing a crucial role, especially for negative emotions.

A major limitation of all these studies is the failure to apply the same paradigm and methodologies to both healthy and pathological populations. This would have offered an interesting comparison of brain dynamics and strengthened the results of my research. Furthermore, my findings sought the temporal and structural neuroimaging correlates, drawing conclusions without considering the potential connectivity between the two hemispheres. To address this issue with my data, one potential solution would be to apply a cutting-edge approach known as atrophy network mapping (Tetreault et al., 2020), which has already been used in the field of lesion studies (Boes et al., 2015; Darby et al., 2017). This method involves using the human connectome to investigate whether certain symptoms or behaviors are associated with specific brain networks. Functional data from a reference group can be used to determine whether lesions in patients, located in different sites but causing similar behaviors, can be mapped into the same brain network.

FUTURE PERSPECTIVES

The present thesis has given rise to a significant new line of research aimed at developing new semantic tasks capable of examining fine-grained differences, spanning all the components of emotion processes to grasp their specificity. Firstly, data collection is still ongoing, with people with semantic dementia undergoing the emotion fluency task. This will allow me to compare the performance of people with svPPA and sbvFTD and it may represent an optimal tool for differential diagnosis. I hypothesize that people with sbvFTD will score lower in the emotion fluency task compared to the svPPA group, which, in turn, may exhibit lower performance on the non-emotional verbal fluency task. Furthermore, an analysis of the valence of the generated words will enhance understanding of the hemispheric lateralization of emotions, investigating whether patients with sbvFTD have significant impairments in emotions or, more specifically, in the negative domain.

As semantic concepts are usually recognized by prototypical features, emotions have distinct characteristics that allow individuals to understand, recognize, and retrieve specific emotion concepts. A new pilot study has been recently conducted in our laboratory, asking 31 participants (15 males, 16 females) to describe an emotion thinking about the situations that might have elicited it, the physiological sensations experienced, and what face, voice, and posture are more related to that emotion. I extracted prototypical features for ten different emotions, five with positive valence (i.e., amusement, awe, sympathy, love, pride), and five with negative valence (i.e., anger, fear, sad, disgust, shame). Based on a study by Catricalà et al. (2013, 2015) on living and non-living concepts, I created a questionnaire where each question includes two-alternative forced choices comprising a target emotion feature and an alternative emotion feature. My aim is to provide the questionnaire to healthy subjects and patients with frontotemporal dementia to assess the semantic knowledge of prototypical features of emotions.

To address the issue, I have also developed a new version of a semantic association task to explore the emotional knowledge of participants by assessing all the concepts within each emotional category, both in verbal (words) and non-verbal (faces) modalities. The idea came from a study by (Cowen & Keltner, 2021), who created topological space maps for both verbal and non-verbal stimuli (i.e., voices, prosody, faces, videos) by identifying distinct clusters and gradients of relatedness falling within the same emotion concept. A cluster, or emotion family, may go by a prototypical label, such as “anger”, and contains closely related states such as irritation, frustration, and rage that can occur in similar situations. The rationale behind this task will be to explore the emotion knowledge of healthy subjects and patients with semantic dementia, assessing their knowledge of emotion categories. Performance of patients with semantic dementia in these new semantic tasks will unveil the brain correlates of socioemotional semantic, taking a step forward in the unsolved debate on hemispheric lateralization of emotion.

APPENDICES

A. **List of Italian words included in the stimulus sets for Studies 1, 2, and 3.** Words are divided into positive words, negative words not associated to pain, and negative words associated to pain and the English translation is reported.

Positive words		**Negative words not associated to pain**		**Negative words associated to pain**	
Italian	**English**	**Italian**	**English**	**Italian**	**English**
Agilità	Agility	Abbandonato	Abandoned	Aggressione	Aggression
Ambizione	Ambition	Alcolista	Alcoholic	Amputazione	Amputation
Ammirato	Admired	Angosciato	Anguished	Atroce	Atrocious
Amore	Love	Annoiato	Bored	Cancro	Cancer
Angelo	Angel	Ansioso	Anxious	Dilaniante	Excruciating
Appetitoso	Luscious	Arrabbiato	Angry	Dolore	Pain
Arte	Art	Assassino	Killer	Ferita	Wound
Atletica	Athletics	Avidità	Greed	Fitta	Stabbing pain
Attraente	Handsome	Avversione	Hatred	Frattura	Fracture
Aurora	Dawn	Bastardo	Bastard	Frustata	Lash
Avventura	Adventure	Bestemmia	Blasphemy	Incurabile	Incurable
Beatitudine	Bliss	Bollente	Hot	Infarto	Heart attack
Bebè	Baby	Bomba	Bomb	Infiammazione	Inflammation
Bellezza	Beauty	Carcere	Jail	Lacerante	Lacerating
Bello	Beautiful	Cattivo	Evil	Lacerazione	Laceration
Capace	Capable	Collera	Anger	Lancinante	Stabbing
Cascata	Waterfall	Colpevole	Guilty	Lesione	Lesion
Cervello	Brain	Corrotto	Corrupted	Male	Pain
Charme	Charm	Criminale	Criminal	Mutilazione	Mutilation
Ciclamino	Cyclamen	Crisi	Crisis	Piaga	Plague
Comfort	Comfort	Debito	Debt	Scorticamento	Flaying
Conoscenza	Knowledge	Demonio	Demon	Sevizia	Torture
Coraggioso	Brave	Disastro	Disaster	Sofferto	Suffered
Cortese	Kind	Discarica	Dump	Supplizio	Torment
Curioso	Curious	Disgustato	Disgusted	Tendinite	Tendinitis
Delizia	Delight	Distruzione	Destruction	Torturante	Torturing
Desiderio	Wish	Drogato	Drug addicted	Trafiggente	Piercing
Diamante	Diamond	Egoista	Selfish	Trafittivo	Excruciating
Dollaro	Dollar	Feccia	Scum	Trauma	Trauma
Dono	Present	Fetore	Stench	Ulcera	Ulcer
Eccellenza	Excellence	Frustrato	Frustrated	Ulcerativo	Ulcerative
Eccezionale	Outstanding	Ghigliottina	Guillotine	Ustione	Burn
Eccitato	Aroused	Grasso	Fat		
Eccitazione	Excitement	Guerra	War		
Elegante	Elegant	Ignoranza	Ignorance		
Erotico	Erotic	Immaturo	Immature		
Estasi	Ecstasy	Immondizia	Dirty		
Esultante	Elated	Impaurito	Scared		
Fantasia	Fantasy	Impotente	Impotent		
Favore	Favor	Incidente	Accident		
Ferie	Vacation	Incubo	Nightmare		
Festivo	Festive	Infedele	Unfaithful		
Fiducioso	Confident	Inganno	Deceit		
Forte	Strong	Inondazione	Flood		
Fortunato	Lucky	Insicuro	Insecure		
Fratello	Brother	Inutile	Useless		
Giocattolo	Toy	Maleducato	Rude		
Gioioso	Joyful	Malvagio	Wicked		
Gioviale	Jolly	Maniaco	Maniac		
Giustizia	Justice	Marcio	Rotten		
Gloria	Glory	Minaccia	Threat		
Godimento	Enjoyment	Miseria	Misery		
Grato	Grateful	Muffa	Mold		
Gusto	Taste	Nervoso	Nervous		
Idea	Idea	Obesità	Obesity		
Idolo	Idol	Odio	Hate		
Incentivo	Incentive	Odioso	Obnoxious		
Interesse	Interest	Omicida	Murderer		
Ispirato	Inspired	Orrore	Horror		
Leale	Loyal	Ostile	Hostile		
Liberazione	Liberty	Penalità	Penalty		
Libertà	Freedom	Perdente	Loser		
Luminoso	Bright	Pericolo	Danger		
Lusso	Luxury	Pessimismo	Gloom		

Positive words		Negative words not associated to pain		Negative words associated to pain	
Magico	Magical	Povertà	Poverty		
Magnifico	Terrific	Precipizio	Cliff		
Mente	Mind	Prigione	Prison		
Meraviglia	Wonder	Putrido	Putrid		
Milionario	Millionaire	Puzza	Stink		
Miracolo	Miracle	Rapimento	Abduction		
Mondo	World	Ratto	Rat		
Natura	Nature	Respinto	Rejected		
Neonato	Infant	Ricatto	Blackmail		
Neve	Snow	Sanguinoso	Bloody		
Oceano	Ocean	Schiavo	Slave		
Onore	Honor	Sconfitto	Defeated		
Orgasmo	Orgasm	Scoraggiato	Discouraged		
Oro	Gold	Sepoltura	Burial		
Ottimismo	Optimism	Sgradevole	Nasty		
Paradiso	Paradise	Sleale	Disloyal		
Passione	Passion	Solitudine	Loneliness		
Perspicacia	Wit	Spaventato	Scared		
Possibilità	Chance	Spazzatura	Garbage		
Prestigio	Prestige	Sporcizia	Filth		
Progresso	Progress	Sporco	Dirt		
Promozione	Promotion	Sudiciume	Grime		
Protetto	Protected	Terrorista	Terrorist		
Radioso	Radiant	Terrorizzato	Terrified		
Regalo	Gift	Traditore	Traitor		
Ricchezze	Riches	Tragedia	Tragedy		
Ricco	Wealthy	Truffa	Fraud		
Ricompensa	Reward	Vandalo	Vandal		
Riconoscente	Thankful	Vigliacco	Louse		
Rinfresco	Refreshment	Vittima	Victim		
Rispetto	Respect	Zanzara	Mosquito		
Romantico	Romantic				
Saggio	Wise				
Sesso	Sex				
Seta	Silk				
Sexy	Sexy				
Sicuro	Safe				
Soddisfatto	Satisfied				
Soleggiato	Sunlight				
Sorpreso	Surprised				
Sorriso	Grin				
Spensierato	Carefree				
Speranza	Hope				
Speranzoso	Hopeful				
Sposa	Bride				
Studioso	Scholar				
Successo	Success				
Talento	Talent				
Tesoro	Treasure				
Trionfante	Triumphant				
Trionfo	Triumph				
Trofeo	Trophy				
Umile	Humble				
Utile	Useful				
Vantaggio	Advantage				
Vigoroso	Vigorous				
Villaggio	Village				
Villetta	Cottage				
Vincitore	Champion				
Virtù	Virtue				
Vita	Life				
Vittoria	Victory				
Vivace	Lively				
Vivo	Alive				

B. Anecdotes from the Chart Review in Study 4.

Behavior	Sub-domains	Quotes
Mysticism	Spirituality	In church, he will think that the person preaching is speaking directly to him, particularly if they know one another on social terms.
Mysticism	Spirituality	She prays for god to take her and says god has told her he is coming for her.
Mysticism	Spirituality	begun to bringing home books from the library on death and dying and reading them to her at bedtime
Mysticism	Spirituality	by mid 2004, he was calling friends and family to report that his wife was not allowing him to serve God, and that their relationship was not good.
Mysticism	Spirituality	experienced visual hallucinations by seeing his deceased parents. He has had delusions that God was giving him the correct lottery number.
Mysticism	Spirituality	has always been a very spiritual person, but she currently feels more connected to her soul/spirit/optimal future self, being more spiritual in general. When asked, she reported that her feelings of happiness and spirituality have increased in the last few years.
Mysticism	Spirituality	she does feel some vibrations in her feet that she feels is coming from God
Mysticism	Spirituality	she feels God is helping them
Mysticism	Spirituality	The patient claims that she has been "saved" and reads the Bible daily and attends church every Sunday, but there are no reports of hyper-religiosity.
Mysticism	Spirituality	The patient has lost interest in reading which she previously enjoyed, including philosophical and spiritual readings, now preferring to be read to.
Mysticism	Spirituality	There was one instance where she held her hand towards a picture of Jesus and the Virgin Mary. She pointed towards Jesus, and exclaimed, "I know him!"
Mysticism	Spirituality	visual hallucinantion of angels. She is not afraid of these visions, but rather pleased.
Mysticism	Spirituality	When asked about her mood, Ms. Graydon states that she is, "Fine and relies on God's help to help her."
Mysticism	Magical Thinking	She listens to more paranormal podcasts. She has gone to a psychic a few times; the psychic previously worked with her when her son was first diagnosed with Lyme. Note: She has a baseline interest in the paranormal, believing her grandparents' house was haunted at the age of 15 years
Mysticism	Magical Thinking	he has a recent preoccupation with aliens and will say, "I think aliens are helping us on computers."
Mysticism	Magical Thinking	He does report that she has always been a very artistic person and has, over the past 2 years, had increased discussion of such things as the clouds "speaking to her", though discussion the meaning of the shapes of clouds would be typical for her baseline personality.
Mysticism	Magical Thinking	developed an odd belief that mermaids were real. On halloween She was dressed as a witch, and she became firmly entrenched in this character, as if it was her true persona. She acted like a witch throughout the day.
Mysticism	Magical Thinking	"healing magic" mentioned in our lab but not neurology note
Mysticism	Connectedness	This had not been of concern to her until recently, when she felt this desire to increase her connectedness with people. Despite a desire for increased connectedness, the patient declines social meetings with friends.
Mysticism	Connectedness	They feel that early on he had some increased emotionality and showed his emotions more. They provide an example of his being concerned about a homeless person, wanting to provide money and not understanding their explanation regarding why not to.
Mysticism	Connectedness	states that she "cares for and prays for and loves everybody."
Mysticism	Connectedness	She prays to God every day and is thankful for her wonderful life, her family and friends, and a healthy planet.

Mysticism	Connectedness	She began speaking bombastically about universal ideals, such as, “justice for all.” She remarked, “We need to save the people. We are all here for others.” began approaching strangers on the street, immediately striking-up conversation. Mike said, “She goes-up to dirtbags on the street… I don’t know why she talks to them.” X responded, defensively, “I think that if we have a happy talk, they could be happier.” Additionally, she developed an increased interest in volunteering. She increased her volunteer commitments to 15 hours per week (previously 3 hours per week).
Mysticism	Connectedness	She also was making poor decisions such as picking up homeless people on the street and offering them rides for long distances.
Mysticism	Connectedness	possible. She had motivation to look for "homes for oprhan items" leading to her hoarding
Mysticism	Connectedness	her husband describes her as “too warm and loving”, further stating that she has always been an optimist and positive person, but now this trait is significantly heightened (“(patient) is relentlessly happy, but this is different, she is tuned in by the beauty of the world around her”). She was very warm and voiced being very grateful of all things. She talked a lot about feeling deep connections with family, friends, me (neuropsych fellow), Will (study coordinator), and “the divine”
Mysticism	Connectedness	He has given his phone number to strangers and one night a woman came to his house, when he was sleeping and his wife answered the door to find out that he had invited her because she needed help.
Mysticism	Connectedness	He frequently uses the words “dead”, “deleted”, and “connected” to describe things
Mysticism	Connectedness	He also began to collect art supplies, textbooks, art pencils, and now collects aluminum bottles and plastic cans to give to the homeless. When asked why he does this, he tells his wife, “Because he might be homeless one day.”
Mysticism	Connectedness	For example, he was moved to tears by seeing the homeless on the street.
Mysticism	Connectedness	daughter caught her talking to homeless people during the pandemic.
Mysticism	Connectedness	"I love people so much because I'm a people person, I'm a people person".
Mysticism	Connectedness	she began to invite homeless people into her house to stay
Mysticism	Connectedness	In addition, she has developed an obsession with political and charitable organizations.
Hyper-religiosity	Religious practices	x's daughters report that also at this time she started using repetitive phrases and would repeat Catholic spiritual novenas while she was crocheting.
Hyper-religiosity	Religious practices	while he has always been religious, he attends morning Men's meeting at church and recently blessed himself in the middle of a meal
Hyper-religiosity	Religious practices	She was not a frequent church goer in the past and now spends a lot of time at Church.
Hyper-religiosity	Religious practices	she has been more preoccupied with religion, buying many things relating to Jesus, saying she is close to Jesus, and praying frequently. She has twenty-plus nativity sets in their living room.
Hyper-religiosity	Religious practices	she has become a bit more religious, playing hymns constantly
Hyper-religiosity	Religious practices	she become hyper-religious, cooking meals every week for her pastor/ at easter, she suddenly stopped eating lunch, pulled out her bible and told her family that she had to pray for them so that they did not go to hell
Hyper-religiosity	Religious practices	She also has expressed more interest in religion, thinking that is an area of great comfort to her and Jesus Christ would be the solution to all of her problems. She sang religious songs a couple of times during the interview.
Hyper-religiosity	Religious practices	raised Catholic. She no longer attends church services; though, she is praying more, especially for her son

Hyper-religiosity	Religious practices	husband reports that they are frequent churchgoers, but she has become "a lot more religious." She performs the "sign of the cross" and prays a lot more
Hyper-religiosity	Religious practices	His Christian religious beliefs have not qualitatively changed, but he seems to be attending church more and seems more religious, according to his wife.
Hyper-religiosity	Religious practices	he started to talk about wanting Jesus to take him away / His religious ideas have intensified and he now is a voracious reader of the Bible and has stopped reading science fiction and other areas. Two years ago he chastised his friends at a Super Bowl party for betting on the game and stopped drinking alcohol for religious reasons. He carries biblical verses with which he criticizes others and cries at sermons.he started to talk about wanting Jesus to take him away
Hyper-religiosity	Religious practices	he did for a time construct a small altar in their home.
Hyper-religiosity	Religious practices	He deplored what he perceived to be his "sinful, immoral" surroundings and resolved to pray and fast for the city's benefit. For over a year he abstained from eating. - Though he has been religious for many years, the intensity of religious fervor and evangelical tendencies have increased in recent years. solid foods for five days a week, limiting his diet to "nutritional liquids" such as chocolate milk.
Hyper-religiosity	Religious practices	Additionally, she started listening to the same music repeatedly, mostly Christian music she has on her iPod.
Hyper-religiosity	Religious thought	When she was asked about her religious interests, she noted that she has always been a religious person. She became tangential, and said, "God created all religions, so they are all good
Hyper-religiosity	Religious thought	The patient was never particularly religious; however, his wife notes that beginning two years ago he began attending Episcopal services every Sunday (he was apparently raised as a Catholic).
Hyper-religiosity	Religious thought	Speaking more freely about her religious beliefs outside of their religious group, something she would not have done in the past
Hyper-religiosity	Religious thought	Since the time of their meeting X has been strongly religious and frequently attended Buddhist Temples, having formally converted from Judaism.
Hyper-religiosity	Religious thought	She occasionally prays for death. She has always been religious, seeing Jesus at the age of 6, but she feels that her relationship with her faith has increased but it is "softer."
Hyper-religiosity	Religious thought	She has had some hyper-religiosity, and notably five-to-six years preceding all of these symptoms did narrow her range of reading to the religious field.
Hyper-religiosity	Religious thought	She has become more religious
Hyper-religiosity	Religious thought	previous medical records increased interest in his religion, but not confirmed by the wife/ mild hyper-religiosity (in the impression)
Hyper-religiosity	Religious thought	Her family also reported a change in religion about a year ago where she converted to being a Jehovah's Witness after she invited some Jehovah's Witnesses into their house.
Hyper-religiosity	Religious thought	He has had no change in religious sentiment, although he did convert to Catholicism at the onset of his illness
Hyper-religiosity	Religious thought	He has become more religious. He always attended church weekly, but now he is a member of a bible study group as well. At church he gets more teary-eyed, but there are no other suggestions of emotional lability.
Hyper-religiosity	Religious thought	He has also developed some rigidity, getting agitated if his routines are disrupted, and being more rigid about attending church. - such as crying when he hears Christmas songs or whenever he goes to church.
Hyper-religiosity	Religious thought	He does become increasingly more emotional, with crying episodes at church, but he has no episodes outside of church.
Positivity	Awe	the sense of euphoria when he is out in nature

Positivity	Euphoria	X became gradually more outgoing, overall friendlier to strangers, and less inhibited in social situations,
Positivity	Euphoria	will approach individuals she doesn't know in social settings so that she can tell them things. For example, will be in a restaurant and will walk over to a couple eating and place her hand on one of the individual's shoulders to tell him how nice the couple looks. In church she will want to walk up to the organist in the middle of service to tell this individual how well she is playing the organ. shakes a person's hand she will often hold onto the individual's hand long beyond what is socially expected. With her grandchildren as well, she will often hold onto them in an embrace even when they are attempting to squirm away. For example, pt has a friend by the name of "x" who has terminal cancer. pt will see her friend on good days and exclaim to the family that x is all better. The sister is concerned pt doesn't seem to understand that her friend isn't going to get better. When asked directly about this, pt states that her friend x is sick. She states she "doesn't want x to suffer".
Positivity	Euphoria	While she was always a friendly person, in the past year or two she has become significantly less inhibited. If she's walking on the street and sees somebody wearing a Yankees cap, she'll shout, "go Yankees!" enthusiastically, sometimes causing the surprised pedestrian to cross to the other side of the street. She also tends to strike up conversations with strangers in public places, asking them questions about themselves and becoming very excited when she finds a commonality.
Positivity	Euphoria	Whereas he was more irritable in the first few years of his symptoms, he became "sweeter" lately, almost childlike
Positivity	Euphoria	When greeting people the patient would start to cry with a strange grimace on his face; he said these cries were expressions of joy. - He mentions that he does not think as much about killing himself and that he has more positive thoughts about what is good in his life.
Positivity	Euphoria	was saying goodbye to acquaintances and being overwhelmingly warm despite obvious cues that this was not desired. Once at a retreat Behaved in an overtly warm fashion towards the other participants (trying to hug them and stating how much she loved them. record comments and concerns from friends over the last three years, including: "she was very different", "had personality changes", and was prone to extreme euphoric emotional reactions" Other complained that she was "taking over conversations: and was "exuding, and telling people that she loved them, but not recognizing the people were uncomfortable. Her prosody is quite striking with high pitch and there a sense of enthusiasm with every phrase, or a declamation-like pattern to her prosody. She expressed having "tears of joy" several times throughout the evaluation, which was accompanied by mild tearfulness. She also often expressed feeling "happy happy happy" in a highpitched, melodic voice while dancing in her seat
Positivity	Euphoria	The patient described herself as a very positive person. Her husband confirmed that she has a positive mood. - The patient has exhibited further changes in her getting to close to people and touching others more, as well as calling strangers "my dear". - Rather impulsively she explained to the attending "Your head is incredible! Your brain!" when looking at his head and hairline. interpersonal interactions, getting to close to people and touching others more, as well as calling strangers "my dear".
Positivity	Euphoria	tends to hug people she doesn't know well (Mrs. X says she hugs only family and friends) and is overwhelmingly positive. - She does acknowledge that her husband may be annoyed with her behavior, but that she is so incredibly in love with him that she wants to do everything that she can to make him happy.
Positivity	Euphoria	talking to strangers including people they do not know/ For instance, on trips, he very frequently offers to take other people's picture using their camera/ In addition, he has a tendency now to approach anyone standing near him and ask them about themselves./

Positivity	Euphoria	subtle behavioral changes, including a childish affect
Positivity	Euphoria	speaks more frequently with strangers, always remaining friendly and appropriate at those times.
Positivity	Euphoria	she would tell husband “I love you” 5 times a day prior to her illness, she now says it >50 times a day and follows that by “I need you.” She also tells her daughters (total of 2) that she loves them rather frequently
Positivity	Euphoria	she would often act childishly, for instance blowing bubbles at her sister despite being asked to stop. who noted disinhibition, elation
Positivity	Euphoria	she will talk about private affairs between her and her husband to other family membersOn one occasion when they were attending a formal dinner, she started singing at the dinner table and embarrassed her husband. In the clinic today, she sang songs, drew pictures of the doctors interviewing her, and invited one of the clinic staff to visit her in Malaysia
Positivity	Euphoria	She will approach perfect strangers in the grocery store and within seconds of asking about some grocery item she is on to talking about how she paints people and their pets and that she inquires whether people are interested in her work.
Positivity	Euphoria	She watches the same TV programmes every day, participularly children's programmes, such as Barney or Dora - became repetativiely concerned about my hands being cold
Positivity	Euphoria	she was quite friendly and affectionate with strangers and would rub men's bellies and demonstrate ballerina tricks and steps to these men/ she often walks around the house naked and even exposed herself to the caregiver once/ on neurological examination, she was quite disinhibited and childlike, reaching out to touch the examiner's face and asking the ages of the examiners. she is also quite animated and at times stands up and sings and shakes the shoulders
Positivity	Euphoria	She was at other times apparently euphoric with inappropriate giggling and a jovial affect. She was somewhat child-like and playful, violated interpersonal space and exhibited mild verbal dysdecorum.
Positivity	Euphoria	She was always a happy and warm person around people, but these characteristics became exaggerated such that she greets and treats those she meets for the first time as if they are lifelong close friends. She once asked strangers on the street to pick up after her dog, which was uncharacteristic
Positivity	Euphoria	she tends to wave more often to babies, who are unknown to her.
Positivity	Euphoria	She smiled frequently. Her affect is sometimes childlike, and she makes short sound effects like “num” or “dop” when doing the physical exam, such as whenever our fingers touch on finger nose finger. - She often repeats the phrase “thank-you” or “how special” without particular context.
Positivity	Euphoria	She seems to be more positive and happy in a childish way and all of the time. She is more talkative than she used to be and more willing to be "touchy" and affectionate than she used to. During the interview today she hugs and kisses her husband repeatedly.During the interview today she hugs and kisses her husband repeatedly.
Positivity	Euphoria	she saw a friend across the street and yelled "that's my lover"
Positivity	Euphoria	She said she is pretty happy and that nothing is wrong and there no problems when asked why she was at UCSF
Positivity	Euphoria	She once did a dance in front of many patrons in a doctor's waiting room. She will frequently approach strangers and talk with them.
Positivity	Euphoria	she is now telling strangers about her life stories. On exam, she is mildly disinhibited and child-like in affect.
Positivity	Euphoria	She is more talkative and friendly with strangers, and will say hello to “anyone…everyone.” she was warm, socially appropriate, and overly jovial.

Positivity	Euphoria	She has not exhibited any socially inappropriate behavior, but is more demonstrative of her affection for him in public (stroking his leg, hugging him him), and is perhaps more gregarious with strangers than previously.
Positivity	Euphoria	She has no sex drive, but she is inappropriately affectionate in public and kisses her husband on the cheek.
Positivity	Euphoria	She has had some impulsive behavior the past six years. she said she does these impulsive things because she is "joking around with people." /She has also impulsively talked with construction workers on the street and has wanted to help with whatever they are working on/ At baseline her personality had been energetic, happy, outgoing and confident, but especially in the last five to six years they have noticed some extreme extroversion and inappropriate behavior, including teasing people and socially inappropriate things such as trying to arm-wrestle strangers/ Initially before starting the interview she giggled inappropriately . Initially before starting the interview she giggled inappropriately and introduced herself as "Joanie Baloney."
Positivity	Euphoria	She feels like she is finally letting her real, true self emerge, and that these personality features were always present. She noted, "I'm coming out more for things that I believe in… I don't care if other people don't like me… I'm only concentrating on positive things… I am who I am and I'm sorry if you can't understand me." Her affect was "giddy."
Positivity	Euphoria	she displayed probably too much affection toward local children, arousing suspicion of some of the local residents/ she had a significant change in her behavioral demeanor approximately 2½ months prior to this evaluation when, at a daughter's wedding, she got up and danced with one of her children.
Positivity	Euphoria	She became prone to sudden bursts of anger alternating with periods of elation/ sharing her opinions on baseball with strangers in the street. She has become emotionally blunted, and prone to fits of giggles.
Positivity	Euphoria	She also notes that he has inappropriate laughter, although does not note inappropriate crying. She also describes some mildly disinhibited behaviors she feels are inconsistent with his premorbid personality, such as he hugging strangers in public or rolling down the car window to wave to strangers.
Positivity	Euphoria	She also began buying butterfly lights at Walmart and giving them out to people that she knows.
Positivity	Euphoria	shares that when he was diagnosed, he said "I could have chosen anger, or I could have chosen sadness, I chose humor so I can laugh all the time." He would also chuckle/laugh all the time at everything. Not inappropriate, but just a lot
Positivity	Euphoria	reports a long standing sense of mild elation. She describes her disease process as "fascinating" and looks at it as "a learning experience."
Positivity	Euphoria	Repeatedly throughout today's interview she reports that she "loves to make people happy."/ At times she came close to the examiner's face to express herself
Positivity	Euphoria	regards to behavior, his wife tells me he is childlike and impulsive. He'll go up to strangers and talk to them if they have a child or a dog. He'll water his neighbor's tree
Positivity	Euphoria	Patient's states, "life is good." In 2012, he began laughing at inappropriate times, such as during sports games
Positivity	Euphoria	Over the last two years, she has begun to point out people somewhat inappropriately in public; she will, for example, point out obese people, or women with short skirts, to her daughter. She has begun to give people a "peck on the cheek" rather than shaking hands when she leaves. She is mildly disinhibited, in that she gives the examiner a kiss on the cheek after her neurologic examination
Positivity	Euphoria	On this journey, he repeatedly sat close to and talked to strangers and maintained loud, animated conversations across a crowded train.

Positivity	Euphoria	noted to constantly wring her hands and tap her feet. There was a child-like quality to her behavior since she constantly giggled (2/27/2018)/ she has had a preoccupation with young men, talking to them in public and saying how nice they looked, and printing pictures of young men. She is not rude, but clearly makes them uncomfortable with her attention. She encourages young men to hug her.
Positivity	Euphoria	Neurologist says She referred to me as "honey" and "baby" multiple times during the interview.
Positivity	Euphoria	neurologist describes slightly disinhibited (dancing when walking, slightly too intimate). She had difficulty recognizing the emotions associated to facial expressions (particularly negative ones such as sadness and anger)
Positivity	Euphoria	more touchy toward her husband. This has only manifested towards him, however. She seeks his physical contact more than before
Positivity	Euphoria	More recently, in the past ten months, the patient has begun to sing a repertoire of eight hymns spontaneously in multiple social situations. she has been speaking freely with children to whom she is a stranger. She is constantly arising and pacing the room. She is oftentimes singing or humming and picking at her fingernails. . She refers to each examiner as "honey".
Positivity	Euphoria	More recently, he has developed an inclination toward singing when attempting to engage strangers.
Positivity	Euphoria	loss of concern over personal boundaries, frequently bumping into people and staring almost inappropriately at strangers/ She was mildly disinhibited and insisted on taking pictures of the staff for what she called "picture of the day"
Positivity	Euphoria	Later in 2005, his wife noted that he was not himself, and began to act "clownish" and not "ageappropriate."For example, he began to care only about what he wanted to do. He would extensively tease his wife and his brother, and would make inappropriate jokes about sex and farting. His wife adds that he would talk to her "like his junior high-school buddy," and at some point drove through his old neighborhood and pointed out each house in which he had sex with his previous girlfriends. In 2005, he began to act very childish in bed with his wife, and his wife refers to him as "a little boy losing his virginity." He has also approached young children with over-the-top enthusiasm. His family began to refer to him as "payaso" which means clown in Spanish. He childishly acted out snoring when asked about his sleep and frequently invaded the personal space of the examiner
Positivity	Euphoria	joyfully hiding from her family behind cars
Positivity	Euphoria	in one instance he hugged his wife 14 times after hearing that "women like affection" in a sermon. He repeated the behavior later because " it made his wife laugh"
Positivity	Euphoria	His wife reports some instances of disinhibition, for example he standing and mock-conducting along to the music at concerts in Golden Gate Park.
Positivity	Euphoria	His wife notes that he is more emotional, suddenly expresses his love to his 17-year-old son, at times actually making his son somewhat uncomfortable.
Positivity	Euphoria	His wife is worried that he is overly friendly with solicitors and invites strangers into the home.
Positivity	Euphoria	his wife describes him as developing the personality of 14-year-old/ he began to talk to people including strangers a lot/ he would particularly like to talk to children and seemed to feel like he was one himself/ he would fight with his grandchildren over who would sit in the front seat/ e began to develop a childlike desire for poeple not to touch things that were his
Positivity	Euphoria	his wife describes child-like behavior, for example he has been putting stuffed animals around the house, he walks around in public with his medals around his neck.
Positivity	Euphoria	his brother noted he has a more childish sense of humour

Positivity	Euphoria	Her overall outlook tends to be remarkably positive about herself, child-like, and without as much regard for others
Positivity	Euphoria	Her neurologic exam was remarkable in the mental status for a cheerful affect,
Positivity	Euphoria	Her husband describes that she tells her life story to strangers. She kisses the hands of strangers and tells him that they are gorgeous. Her husband describes she is very happy. She was always a cheerful warm person and her husband describes that her personality is the same, but magnified.
Positivity	Euphoria	Her daughter says that she is more lighthearted, and sings and dances more. She is less inhibited but only in a socially appropriate way—she is less reserved than she used to be, for example dancing with others at a party in China.
Positivity	Euphoria	Her behavior has become childlike and "sweet" to a certain extent, with an openness with strangers she did not used to have
Positivity	Euphoria	He's always been an outgoing and gregarious person, and he has never had difficulty speaking with strangers, but he spends more time speaking to strangers. Erika says, "He stops to talk to everybody."
Positivity	Euphoria	He would invite people who were walking by their house, whom he did not know, to come and have a tour of his house
Positivity	Euphoria	he would also laugh inappropriately in many situations in a way that his wife characterized as "nervous laughter". This has a giggly and silly type of quality
Positivity	Euphoria	He was very playful during the examination. When asked to say "ah" he sang a tune. When asked to whistle, he whistled the Indiana Jones theme song. When completing supination/pronation he tapped out a melody. He made melodies/sounds to accompany his movements when putting on his shoes
Positivity	Euphoria	he was a bit over-excited at a wedding, with a lot of clapping and was saying it was the best wedding he'd ever been to, in a childish way/ says that he doesn't have a problem, and that he's coming because his wife "does wonderful things that she does".
Positivity	Euphoria	He talked to strangers more than before and asked them where they were from or how long they lived here.
Positivity	Euphoria	He offers that he is content to sit and look at the bay for hours and feed the birds, and is somewhat surprised by this.
Positivity	Euphoria	he laugh at most things in most situations, often inappropriately
Positivity	Euphoria	he is making more jokes than he has in the past
Positivity	Euphoria	He is described as laughing more often now. His personality is unchanged, but old traits seem to be exacerbated now, such as his increasing wordplay. He frequently makes puns and plays with words-- for example, when told to Google something, he says "Barney goo-goo googly eyes
Positivity	Euphoria	He has become more jocular and, in the past six to nine months, has begun to tell jokes to strangers in public places. According to his wife, he will oftentimes repeat the same joke.
Positivity	Euphoria	He has also begun to hug people inappropriately in situations like this. For instance, recently he hugged the woman standing in front of him in line at Costco.
Positivity	Euphoria	He had euphoric affect and he would often giggle and laugh.During his visit with us, his behavior was described by various providers as inappropriately jovial
Positivity	Euphoria	he had become more gregarious.In the past year his wife believes that his mood is much happier.His wife feels that although he is more likely to approach and hug and sometimes kiss strangers, overall he lacks warmth. She also feels that sometimes he is silly in a childish way which is new.
Positivity	Euphoria	He feels he speaks less than usual though his wife thinks that he talks more and he might walk up to strangers and talk to them. She feels this is new and a change in his personality. He also may change his voice on the phone for a prank. This started around 2 years ago.

Positivity	Euphoria	He calls most people "sweetie" and often will want to touch them or rub their back, and more recently has begun to try to kiss them in a nonsexual way. He has also on occasion asked his caregiver to lay in bed with him because he does not want to be in bed by himself when his wife is away. Again, there is no suggestion that this is particularly of a sexual nature. His daughter describes him as having increased "sappiness"; he will have an occasional tear with this. The patient is described as a "wild child"
Positivity	Euphoria	he began to develop a more juvenile sense of humor with emphasis on puns and plays on words.
Positivity	Euphoria	He became overly happy and joked more. At this time, x called him “Uber-X” and now uses this term to refer to him when his baseline extroversion is heightened
Positivity	Euphoria	He appeared pleasant and cheerful with an inappropriate euphoric affect, and he frequently smiled broadly.
Positivity	Euphoria	has begun hugging strangers, in particular policeman. jumped on the back of a stranger wearuing a horsehead costume and interposed himself onto the stage during a performance. Hugging strangers. He is drawn to light-hearted romantic movies, whereas he used to love the sopranos.
Positivity	Euphoria	had the engaging demeanour of a teenage boy, frequently making gentle jokes and indulging in slightly mischievous behaviors.
Positivity	Euphoria	giggles inappropriately/ referred to the neuropsychology student as her "cutie"/ Her son notes that she likes to whistle to the same tune ("you are my sunshine") everyday continuously, and also likes to pace around the house continuously saying "yeah, yeah, yeah" to herself.
Positivity	Euphoria	excessively excited over small things like running into someone in the store/she also put her hand on her daughter's boyfriend while talking to him in a manner that showed lack of respect for social boundaries/ childlike demeanor/ approach stranger in store/ less respect for personal space
Positivity	Euphoria	described as havin become very friendly toward strangers. He will touch people on the shoulder or back that he does not know. He will tap on the window of his car to wave to people in the next car that he does not know. Would speak in work play such as using puns or rhyming
Positivity	Euphoria	daughter thought she was behaving more childish with her (daughter's) children
Positivity	Euphoria	child-like behavior (involving cheerful expositions of scripted speech and yoga maneuvers)
Positivity	Euphoria	Behaviorally, Mrs. X is more warm and loving than she used to in the past. When sitting in a restaurant she will approach strangers and offer up topics of conversations that include money, weight, or age, or otherwise give unsolicited advice.- She thanks random people for their service. - Her speech is childlike
Positivity	Euphoria	began to refer to people as "cutie" or "darling - or "I like to have fun fun fun"
Positivity	Euphoria	began talking to strangers and trusting people she did not know. laughs and cries inappropriately and is sometimes emotionally labile. Often gets up to demonstrate a dance or activity
Positivity	Euphoria	began generating jokey, offensive nicknames for his friends. He was playful and sometimes had a child-like demeanor
Positivity	Euphoria	at neurological examination she is pleasant to the point of euphoria, she was jocular and at times inappropriate/ prone to engage in conversations with strangers/ particularly interested in talking to children and began touching them even she doesn't know them
Positivity	Euphoria	approaching strangers and talking to them about intimate details/ The family did not necessarily notice anything strange right away because X has always lived a very unconventional life- raising her kids on a "hippy" commune in Mexico- and often saying unconventional socially unacceptable things and doing impulsive things to help people her whole life

Positivity	Euphoria	approaches strangers in dangerous areas and walks into homes when accompanying her husband delivering furniture.
Positivity	Euphoria	A concerning event for his wife, that led to his evaluation in a clinical setting by Dr. X, was in 2011 when they were at a festival together and he went up to a judge at the Bunny Barn while she was working and started a conversation/ talk to other out of place in social settings
Positivity	Euphoria	4-1/2 years into the course of his illness, he began compulsively approaching strangers to ask about their birthday and the state in which they were born. He also began offering backrubs to everyone he encountered, including strangers/ His affect was jovial and even giggly at times. in 2005 His affect is almost joyous and he will often laugh/ He often holds on to people's hands.
Positivity	Euphoria	she laughs frequently and approaches people on the street
Positivity	Euphoria	In addition, during our interview today she spontaneously stated, "I don't sleep with other men." Mrs. Colombo is more extroverted now and will talk more readily to strangers.
Positivity	Expansiveness	When she presented to clinic, she was dressed extravagantly in several shades of purple. She wore carefully applied heavy makeup. While waiting for examination, she danced and involved many people in conversations about her appearance and the jewelry she wore. she repeatedly stated that the various people in the clinic "loved her."
Positivity	Expansiveness	There is also possible evidence of mild grandiosity, such as when he declared in the interview "I can run from here to China without stopping."
Positivity	Expansiveness	The patient also began to write his own informal "personal memoirs" of his life in late 2004.
Positivity	Expansiveness	she will frequently approach strangers and introduce herself as a world famous author, and sometimes strangers are not particularly receptive to her intrusions.
Positivity	Expansiveness	She will approach perfect strangers in the grocery store and within seconds of asking about some grocery item she is on to talking about how she paints people and their pets and that she inquires whether people are interested in her work.
Positivity	Expansiveness	she was wearng ballet slippers and pranced around the thous and shook her shoulders saying "I'm a ballerina"./her son took her to a café and she was giggling and telling her son that she was going to be a singer on TV, perhaps on American Idol.
Positivity	Expansiveness	She typically started by telling a set of facts that she referred to as "her life story"
Positivity	Expansiveness	she often loudly discusses the importance of her daily practice of using a vibrator to achieve "a real orgasm." She also has been having sex with men whom she meets online, again in part with the intention of making them like her. During the interview today she proudly and repeatedly declares that she has turned down exchanges with teenage boys, saying to no one in particular, "No! I won't cougar you!"
Positivity	Expansiveness	She noted "I'm an artist"
Positivity	Expansiveness	She is still carrying around sheet music for pianos she may encounter, however, she now has less regard for situations and will spontaneously start playing (hotels, etc.). For both of these activities she comments how appreciative others are of her.
Positivity	Expansiveness	She has become more selfish and self-centered, demanding all of her husband's time and becoming jealous when he is away to work or spending time with his family. In fact he reports that she "caused a scene" once when he was playing catch with his granddaughter and demanded that he spend time with her.
Positivity	Expansiveness	She has become boastful, telling everyone that she is "perfect."
Positivity	Expansiveness	she had developed mild changes in personality, including a more domineering style with her children
Positivity	Expansiveness	she developed a new obsession with writing a screenplay which she told everyone would make her famous
Positivity	Expansiveness	said everyone on the cruise ship knew who she was

Positivity	Expansiveness	on a family trip, he was found to be very harsh and belligerent toward his 13yo nephew, exhibiting shownmanship and picking on his weaknesses
Positivity	Expansiveness	In restaurants he always stops and talks to strangers and will beguile them with grandiose stories about two-million-dollar electrical contracts
Positivity	Expansiveness	His self-centeredness has been noted, for instance, in situations where he will be talking to a family member like his daughter, and if something happens such as milk spilling on the floor or one of children coming in with a skinned knee, he will ignore this event and continue to talk with his daughter about whatever they were discussing
Positivity	Expansiveness	His brother has also noticed that he has been more boastful. He has not dated any women since he has come to the United States, but approximately two months ago he was boasting to his brother about a girl he had dated in Russia and telling him about sexual intercourse with her
Positivity	Expansiveness	Her typical topics tend to focus her impressive personal accomplishments and impressive accomplishments of her ancestors
Positivity	Expansiveness	he was always very confident of himself, but he began to tell others without a stimulus how he was "brilliant" a behavior that was out of character for him
Positivity	Expansiveness	He talks inappropriately loud in public, and gives too expansive a response when he is asked a question, but does not do too many other inappropriate things in public
Positivity	Expansiveness	He started to brag about his clarinet skills, an instrument that he has played since he was 10 years of age. He began to boast about how he was the best player in the band, and that he was the conductor's favorite player. Although he always had an interest in music, he became obsessed about improving his skills, and insisted that he never should miss a concert. He also started becoming more gregarious in public, and the topic of the conversation centered around his musical abilities, or around the talents and salaries of his children.
Positivity	Expansiveness	He previously was very reserved and private about his money. However, he now close about the money that he spent and loves to discuss his purchases. He never used to allow his daughters to even show cash in public, but now openly flaunts his net worth.
Positivity	Expansiveness	He loves telling stories from his childhood and about his earlier married years.
Positivity	Expansiveness	he had become more gregarious as well as boastful of his accomplishments/ He has a tendency to talk repeatedly about his previous career in international business, saying "I was number one".
Positivity	Expansiveness	he began to be slightly more inappropriate and attention-seeking during public events
Positivity	Expansiveness	has been displaying increased grandiosity. She talks about her children and grandchildren as if they have a supernatural ability to shape the future. For example, she noted, "Megan and husband are the couple of the future."
Positivity	Expansiveness	four-to-five years ago that she decided to have a change in her career to become a music businesswoman or producer
Positivity	Expansiveness	Behaviorally he exhibited verbal dysdecorum, lack of insight, self-centeredness (with frequent use of the word "I") boastfulness and grandiosity.
Positivity	Expansiveness	At times, he was boastful and, at other times, was very self critical (during the evaluation)
Positivity	Expansiveness	at neurologic testing, his behavior was boastful and grandiose
Positivity	Expansiveness	Around this time, she also developed exhibitionism as manifested by her dressing in gym outfits at inappropriate times or showing off her muscles by flexing in public
Positivity	Expansiveness	approach others more intrusively/childlike in wanting attention/her daughter describes her as a "wounded teenager"
Positivity	Expansiveness	. He frequently, and sometime uncomfortably, takes out a picture of his grandson to show it to anyone he can.

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