INTERNATIONAL JOURNAL OF PSYCHOLOGY AND NEUROSCIENCE

From attention to memory in the older adult and Alzheimer's Disease: An integrative suggestion

Da atenção à memória no idoso e na Demência de Alzheimer: Uma abordagem integrada

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REVIEW

Abstract

In the last decade a vast research has been made to understand emotional processes related to attention and memory. This research has focused on the young adult and the elderly as well as in neurodegenerative diseases such as Alzheimer's disease.
In this paper we will explore the relation between attention, memory and emotions, more deeply in the elder adult and in Alzheimer's Disease. We have the purpose to discuss some methodological questions in this research area and provide some possible new ideas to better understand these patients.
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Keywords: alzheimer's, emotional memory, attention, ERP.

Resumo

Na última década tem sido realizada uma vasta investigação por forma a compreender os processos emocionais relacionados com a atenção e memória. Estes trabalhos têm-se focado no jovem adulto, no idoso, assim como em doenças neurodegenerativas como a Demência de Alzheimer.
Neste artigo exploramos a relação entre atenção, memória e emoções, mais profundamente no idoso e na Demência de Alzheimer. Temos como objetivo a discussão sobre algumas questões metodológicas nesta área de investigação, e sugerir possíveis novas ideias que levem à compreensão destes doentes.

Palavras-Chave: alzheimer, memória emocional, atenção, ERP.

Introduction

Due to social, personal and family implications, Alzheimer's Disease (AD) is considered a serious problem in the actual society. The Alzheimer's disease International Association (2013) estimates that there are actually about 36 million of cases diagnosed all over the world. It has being reported that in 2050, this prevalence will be about 115 million. Facing the fact that today we don't have efficient ways to treat or prevent AD, there is a huge need to develop new intervention methods, which allow, at least, a slower progressive degeneration. Many studies were done aiming to understand how to change behavior (e.g. Lancioni *et al*., 2011), social skills (e.g. Lancioni *et al*., 2014), emotional dimensions (Ozdemir & Akdemir, 2009) or in general quality of life (e.g., Terada *et al*., 2013) in AD patients. Other studies have focused in neurocognitive domains like attentional processes (e.g., Romberg, Bussey, & Saksida, 2013), memory (e.g., Gallo, Foster, Wong, & Bennett, 2010) or executive function (e.g. Marshall *et al*., 2011). Concerning to these neurocognitive studies, with normal populations, it is well established that more attention to certain kind of stimuli means consequently better memory to those same stimuli or its properties (e.g. Kensinger, 2009; Weymar, Löw, & Hamm, 2011). The type of stimuli that can be more relevant to human being is also a matter of research. According to Schupp *et al*. (2003) and others, the stimuli relevance is determined by a biological dimension, and is automatically selected by the emotional properties. The emotional significance becomes an important marker to stimuli or events, and guides the selective attention (Lang, Bradley, & Cuthbert, 1997; Öhman, Flykt, & Esteves, 2001, as cited in Compton, 2003), and in this way, if only some information can be attended, it is adaptive to give the priority to the stimuli that directly affect our objectives achievement, in a positive or negative way (Compton, 2003).

Through Event Related Potentials (ERP's) analyses, and using the International Affective Picture System (IAPS), (Lang *et al*., 2008), there is a consensus that in young adults all emotionally charged information has priority in the attentional circuit compared to neutral stimuli (e.g., Rozenkrants & Polich, 2008). Specifically in the emotional stimuli, the ones that have negative valence and a high arousal are the ones that are faster processed. These results expressa human tendency to increase the attention more to unpleasant than to pleasant stimuli in a wide range of dimensions (Cacioppo & Berntson, 1994; Rozin & Royzman, 2001; Taylor, 1991, as cited in Olofsson *et al*., 2008), which had been related to amygdala's faster processing of the aversive information (LeDoux, 1995; Morris *et al*., 1998, as cited in Olofsson *et al*., 2008). Thus, unpleasant stimuli produce stronger emotional effects when compared to pleasant ones being this phenomenon called the *negativity bias*.

Other studies have focused on the different semantic categories of the IAPS. Using (ERP's), stronger responses were found to threat or mutilation stimuli, and to erotic pictures. These results were associated with the arousal. Arousing pictures, pleasant or unpleasant, which are related to primary motivational imperatives, produce stronger responses (Schupp *et al*., 2004).

In older adults and specifically in AD patients there is some controversy concerning what stimuli or properties are more relevant to attentional and memory processes. The complexity seems high since the fact that in the older adult exists a cortex atrophy (Schuff *et al*., 2012), including limbic areas like amygdala (Cassidy & Gutchess, 2012) that is exacerbated in AD patients (Poulin *et al*., 2011).

With this article we will try to make a review focused in attentional and

memory processes in AD patients and healthy older adults. Our aim is to propose a new approach of emotional memory study in AD based on emotional stimuli. This is the first step to understand what stimuli can be used in a more efficient method of declarative memory intervention.

To locate relevant studies, we conducted database searches in the ISI Web of knowledge, EBSCO Publishing and Elsevier electronic databases; only studies in the English language were included. The final search for this review was carried out in July 2014. The keywords used for the search were, 'Attention' 'Emotional Memory', 'International Affective Picture System', 'Affective Norms for English Words' 'Familiarity' 'Recollection' 'P300' 'FN400' and 'Late Positive Complex', combined with each of the following terms: 'Alzheimer's Disease', 'Older adult'.

Attentional Process in the Elder

In the attentional processes of the older adult there is a different functioning mode, occurring changes in the *negativity bias*. In one hand, elder apparently display less physiological arousal whenexperiencing unpleasant emotions. On the other hand, comparing to youngers, older adults selectively attend more to pleasant stimuli (Charles, Mather, & Carstensen, 2003; Isaacowitz, Toner, Goren, & Wilson, 2008; Kennedy, Mather, & Carstensen, 2004; Lai *et al*., 2010; Mather & Carstensen, 2003).

This positivity effect suggest the influence of emotion on attention, and other studies (Charles, Mather, & Carstensen, 2003; Isaacowits, Toner, Goren, & Wilson, 2006; Kennedy, Marther &, Carstensen, 2004) clarify this influenceshowing more sustained attention to pleasant than tounpleasant stimuli. Consequently, it may be considered that*positivity effect* seems to be related to a motivational shift in the emotional

information processing, specifically since it is observed in a readiness way, when older adults have cognitive resources available to the emotional information processing (Mather & Carstensen, 2005). This fact seems related with older adults reports of lower rates of depression, higher rates of positivity affect, and a higher perception of the importance of satisfying relationships (Carstensen *et al*., 2000, as cited in Wood & Kisley, 2006) can occur due to the fact that:

1) The older show less reactivity in the amygdala during the processing of negative emotional stimuli - this can be related as a result of changing goals and shifting priorities, which reduce the salience of stimuli (Samanez-Larkin & Carstensen, 2011).

2) Comparing to young adults some authors defend that in the older does not exist an inferior amygdala activation to unpleasant stimuli, which is similar to what was found in young adults, but there is a high level of amygdala's response to emotional pleasant stimuli (Iragui *et al*., 1996; Mather & Carstensen, 2005). Other authors suggest that in the older there is an elevated attention to pleasant stimuli, which can be balanced with the attention to unpleasant stimuli (Kisley, Wood, & Burrows, 2007). This fact seems to be more consistent with studies referring only a very tenuous atrophy in the amygdala as a consequence of age progression (Mather & Carstensen, 2005);

3) At the same time, when compared to young adults, elders tend to focus more in self-control of experienced emotions (Mather & Carstensen, 2005), as well to dissipate negative emotional states with more efficient ways (Carstensen at al., 2000, as cited in Mather & Carstensen, 2005).

This point is explained by the *Socioemotional Selectivity Theory* (Carstensen *et al*., 2003) who sustains that

this shift seems to be related with a motivation to maximize emotional goals as one's perceived remaining lifetime becomes shorter (Carstensen *et al*., 2000). The top-down changes in motivation seems to play a substantial role in functional changes observed in the aging brain (Samanez-Larkin & Carstensen, 2011). Therefore, the differences found between young andolder persons seem to derive from "top-down" and "bottom-up" changes.

In studies using the IAPS, through ERP's analyses, we can observe this functional mechanism. Kisley, Wood, and Burrows (2007) observed a small decrease in pleasant stimuli amplitude comparing to the amplitude to unpleasant stimuli, and not an increased amplitude to pleasant stimuli. What seems intact in the elderly is the response to emotional stimuli comparing to neutral ones, and like in younger subjects, unpleasant or pleasant stimuli have a stronger response in late positive potentials (LPP) (Kisley, Wood, & Burrows, 2007). Otherwise, for instance, Samanez-Larkin and Carstensen (2011) show that elder subjects give more relevance to pleasant stimuli in a very initial phase of the information processing. However, as referred, this high relevance to pleasant stimuli doesn't imply a less attentional allocation to unpleasant emotional stimuli, and in this way it can be observed an intense attentional response to unpleasant stimuli in the elder, including the fear-inducing ones (Mather & Carstensen, 2005). What seems to happen is that the negativity bias magnitude decreases as age advances and there's an age-related reduction in responding to unpleasant images a gradual, but consistent, linear decrease since 20's, continuing until late life (Kisley, Wood, & Burrows, 2007).

Concerning to semantic categories of IAPS, as far as we know no studies were done in this field with older populations.

Memory Process in the Elder

Following attentional processes, we have other high-order cognitive functions, where memory processes are included. From the very first attention stages, emotional-inducing properties of the stimuli will work as a trigger towards the central nervous system (CNS) activation and will interfere with memory. The information about the emotional load of an experience is usually delivered to the neuronal memory systems such as the hippocampal formation, and can affect memory-related processes in these regions (Richter-Levin, 2004). Research has tried to identify what emotional cues are more or less relevant in the experience, in order to transfer only significant events into the long-term memory. Richter-Levin (2004) suggests neuromediators activated by the emotional load of the experience that are related with memory processes in specific areas like hippocampus, improving the information consolidation. Theseand other authors conclude that when memory is enriched with emotional information becomes more persistent, resistant to disruptions, or more accurate (Richter-Levin, 2004).

For example, some studies suggest that declarative memory to emotional stimuli (pleasant or unpleasant) is typically better than memory for neutral stimuli (Fleming *et al*., 2003; Phelps, LaBar, & Spencer, 1997; Kensinger *et al*., 2002; Hamann, 2009; Mather & Nesmith, 2008; Steidl *et al*., 2006). Overall, this successful memory to emotional stimuli seems syntonic with an increased amygdala modulation of visual processing during encoding (Hamann, 2009). Amygdala's atrophy that occurs in normal aging does not seems to be sufficient to change this emotional effect to memory enhancement (Kensinger at al., 2002). In the elder, in spite of these mild atrophies, the limbic system stays quite preserved (e.g., Insausti, Inausti, Sobreviela, Salinas, & Martinez-Peneuela, 1998, as cited in Kensinger at

al., 2002), resulting in a symmetry between young subjects and elders concerning memory to emotional stimuli, in which both benefit from the emotional properties of the stimuli, including valence (Kensinger at al., 2002).

Concerning to emotional properties of the stimuli, Mather and Sutherland (2009) defend that location memory was better for arousing pictures than for the non-arousing ones. Location memory seems worse for pleasant pictures compared to unpleasant ones. In the same way, other studies found that unpleasant stimuli seem better recalled than those that are neutral orpleasant (e.g., Canli, Zhao, Brewer, Gabrieli, & Cahill, 2000 as cited in Eldstein *et al*., 2005; Kensinger, 2009). Nevertheless, similarly to what happens in attentional processes, there are some doubts about *negativity bias* in the older. For example, Larson and Steuer (2009) found that older showed similar patterns of emotional enhancement effect on the memory, but had better performance for pleasant and neutral stimuli while recalling emotion-inducing words. In the same way Lecler and Kensinger (2011) suggest that older adults retrieve more positive information. Concerning to arousal, this property interferes with memory in a clear way, with evidences that a memory increase occurs to high arousing information (Kensinger *et al*., 2004). Accordingly, a study by Kensinger (2008) shows that a *positivity effect* may occur with more readiness to high arousing stimuli, while older and young adults may remember, in the same way, high arousing stimuli, despite their valence (Mickley & Kensinger, 2009). Regarding this point, it is important to refer that Mickley and Kensinger (2009) suggest that another relevant feature is the self-relevance of the material. This are states where individuals may evidence a tendency to remember pleasant experiences with detail, when these have a close connection with their self-concept. However, they also evidence a tendency to remember negative

experiences with detail, even if these are less relevant at a personal level.

Summing, what was found in memory studies is not consistent, and these results can be derived from the usage of different methods to analyze attention and memory, including the type of stimuli used. Later in this work, we will expose some hypothesis focused on this subject.

Alzheimer's Disease

In AD most of the studies with emotional stimuli were focused on memory. Although, there is some studies focused in the attentional processes and information processment to emotional stimuli (e.g. Boller *et al*., 2002). These studies show that AD patients experience an emotional influence over attention. LaBar, Mesulam, Gitelman and Weintraub (2000) refer that the emotional content of the stimuli occurs previously to the first saccade (before 300ms). They conclude that there is a fast codification to emotional stimuli and a visual orientation and sustained attention to this information in AD patients, at least in the first stages of the disease.

Specifically in AD, due to a large amygdalae's atrophy (Mori *et al*., 1999) there are doubts about the influence of the emotional stimuli in memory. However some studies have found an emotional memory recall influence, and Kensinger *et al*. (2002) suggested more studies to understand the valence and arousal weight, as well as the effect of self-relevance of the stimuli. This idea was shared by LaBar *et al*. (2005), who suggests more research to understand in which way a pleasant valence or the arousal can be more or less affected in AD.

Most memory studies in AD have focused on the recall.There are differences concerning to emotional memory between healthy older adult and AD patients, which already occur in the initial stages of the AD (Kensinger *et al*., 2002). Actually, there are doubts in which way the weight

of different properties of the emotional stimuli, like valence or arousal, can predict differences found between healthy older and AD patients in memory recall (e.g., Kazui *et al*., 2000). In a study conducted by Hamann *et al*. (2000) using IAPS stimuliit was found a difference in AD patients related to emotional stimuli. Comparing to healthy elder, AD groups show significantly less information stored, intact emotional memory to pleasant stimuli, but the memory to unpleasant stimuli seems affected. This positivity effect was not sustained in the recognition task, and was not transported to long-term memory. Authors seem as well to have doubts in intrinsic emotional properties of the stimuli and suggest that certain emotional stimuli – pleasant or unpleasant – may have been particularly memorable.

Kensinger *et al*. (2002) show that AD patients evidenced a tendency to recall more pleasant than unpleasant words, consistent with the relative preservation of memory enhancement to pleasant stimuli at AD. However, in the same study, using visual emotional stimuli, older adults and AD showed reduced memory enhancement based on emotion. Even so, this study reveals a better recall to unpleasant stimuli compared to neutral ones in healthy older, but not in AD. Hamann, Monarch and Goldstein (2000) found a positivity effect only in recognition tasks. Fleming *et al*. (2003) found contradictory results. Using verbal emotional stimuli, the authors refer that AD patients have a better immediate recall of emotional stimuli, specifically unpleasant words. No positivity effect was found.

However, all of studies used different stimuli, different methods, and different levels of disease progression. Inconsistent results were found and actually it is still hard to identify what kind of emotional stimuli can predict more or less immediate or long-term memory in AD.

Besides all research with explicit recall of emotional stimuli, less importance

has been done to familiarity and recollection in AD. According to dual process theories of recognition, we can distinguish two different processes: familiarity and recollection (e.g. Curran & Cleary, 2003). Familiarity is generally thought to reflect an assessment of the global similarity between studied and tested items (e.g. Clark & Gronlund, 1996; Gillund & Shiffrin, 1984; Hintzman, 1988; Humphreys, Bain, & Pike, 1989; Murdock, 1982, as cited in Curran, 2000). Recollection entails the retrieval of specific information about studied items, such as physical attributes (Chalfonte & Johnson, 1996; Hintzman & Caulton, 1997; Hintzman & Curran, 1994, as citedin Curran, 2000). Familiarity and recollection can be measured using ERPs, and with this method it seems that recollection and familiarity are qualitatively distinct (Yu & Rugg, 2010; see Rugg and Curran, 2007, for a review of ERP studies). Familiarity is characterized by a frontal old/new effect (300-500ms) (e.g. Rugg *et al*., 1998; Curran, 2000; Curran & Cleary, 2003; Mecklinger, 2000, as cited in MacKenzie & Donaldson, 2007) and a left parietal old/new effect (500-700ms) varies in a manner consistent with recollection (Curran, 2000; Donaldson & Rugg, 1998; Wilding & Rugg, 1996).

AD patients seem to perform poorly on tasks in which free recall is necessary to oppose familiarity-based false recognition. However these difficulties can be explained by an extreme retrieval impairment since first stages of AD, and this can be verified with a better recognition than recall usually found in AD (Bartok *et al*., 1997; Hamann, Monarch & Goldstein, 2000). If recognition is better than recall, this means that AD patients can memorize some particular stimuli, but they just can’t recallthese memories. Most studies in this domain (e.g. Borg *et al*., 2011) have focused in the total recall of items previously exposed and studied; however

with this strategy the recall is assessed without assessing familiarity and severe impairments are expected in AD patients by primary PFC dysfunction, which is related with retrieval impairments (Abe *et al*., 2011), beyond the present temporal deficits.

As mentioned before, familiarity and recollection without a conscious retrieval can be studied using ERP (e.g. Curran & Cleary, 2003; Speer & Curran, 2007; Yu & Rugg, 2010). In these type of studies an old/new effect paradigm to some stimuli is used which enable the analyzes of the stimuli's emotional influence on attention and memory. Unfortunately these studies have been conductedonly with young populations and older healthy subjects. In AD patients, these types of studies can be particularly useful to understand all memory processes of encoding, storage and information retrieve, as well to understand what kind of stimuli and affective property can influence memory in each moment.

Conclusion

It is consensual that emotional stimuli are easily memorized compared to neutral ones, in all ages. In the elder, there's a *positivity effect*, or in a similar way, a decrease of the *negativity bias*, which seems to be related with a different emotional regulation process, and with a less prominence of the amygdala, that suffers a slow but progressive atrophy with age, particularly in AD. The results in AD patients are not consistent, suggesting no differences between stimuli properties, which seem related with a fast forgetting of all studied information. However, some authors found a slight increase in memory for pleasant stimuli and unpleasant ones. Other studies suggest that words seemed to be better memorized than pictures.

As we can verify there are some inconsistencies in the results. In our opinion these can be influenced by some variables crossing emotion perception to memory access.

In one hand, emotional perception is probably the most important variable because further analysis focused on cognitive domains like attention or memory lies in the emotional stimuli perception. Today, there are some doubts about emotional stimuli ratings of arousal and valence in the older adult and in AD patients. Some studies found that older adult, compared to younger, rate unpleasant pictures as less arousing (Mather *et al*., 2004, as cited in Wieser *et al*., 2006). Other studies indicate that older participants rate pictures as more arousing and more negatively valenced (Smith *et al*., 2005b, as cited in Wieser *et al*., 2006). Gruhn & Scheibe (2008), using 504 IAPS pictures, found that the elder maintain similar responses in valence, meaning that elder and young adult consider in the same way what kind of stimuli is pleasant or unpleasant. However, elder usually classify unpleasant and pleasant stimuli as more arousing, when compared to young populations. This suggests that older people maybe have a tendency to respond more extremely to emotion-inducing pictures.

On the other hand, as referred previously, the inconsistent results probably lies as well in the stimuli modality. Literature suggest that there are age-related changes in amygdala and prefrontal cortex (PFC) recruitment during the processing of emotional stimuli, and the nature of those changes can differ depending on the type of stimulus that is being processed, specifically pictures or words (Leclerc & Kensinger, 2011). Pictures tend to be processed faster than words (Kim, Yoon, & Park, 2004), and to induce activity within emotion processing regions at earlier time points than do words (Schacht, 2008, as cited in Leclerc & Kensinger, 2011). Adopting this criterion, the emotional coding of pictures seems to be evoked more automatically, whereas emotional activation to words may require more controlled processing. Some studies (e.g. Leclerc & Kensinger,

2011) indicate that older subjects show a positivity memory effect to words, but not to pictures, and the way as PFC processes are recruited during codification of distinct stimuli seems to be different in the elderly. More specifically, older adults show an increased medial PFC recruitment to pleasant words, but an increased amygdala activity to pleasant pictures. These data suggest that *positivity effect* in older adults may be related with their recruitment of PFC processes to pleasant information, rather than to enhancements in their recruitment of the amygdala (Kensinger & Schacter, 2008). As a result, more research is needed to understand the differences found in emotional perception and emotional processing between studies.

Concerning to memory most of the studies in AD have focused mainly in recall tasks. With this method and due to initial PFC deficits some information memorized cannot be measured. Better results using recognition tasks support this idea. We suggest more studies focusing on recognition and familiarity to avoid these frontal deficits. ERP analysis allows familiarity and recognition measure and as far as we know, only one study (Boller *et al*., 2002) has used ERP to assess emotional memory in AD.

Therefore, in one hand, the emotional memory different results can be related with the stimuli modality used (words or pictures) or the emotional stimuli properties (different valence or arousal). On the other hand, the access to information memorized has high interference of the frontotemporal structures that are affected since first stages of AD.

We suggest an integrative study of emotional memory stimuli in AD. In our point of view we need to follow the information processing course. First emotional perception to emotional stimuli needs to be controlled. Instruments like IAPS or ANEW should be validated to elder being these results compared to AD patients. Perception is highly influenced at

least by two factors that need to be controlled: cognitive deficits and psychological symptomology. Posteriorly to perception, attention and memory to emotional stimuli can be measured with techniques like ERP. Few studies were conducted to assess attentional allocation to emotional stimuli in AD. Familiarity and recollection can be analyzed avoiding free recall and PCF deficits usually present in AD patients.

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How to cite this Article: Sousa, H., Marques-Teixeira, J., & Barbosa, F. (2015). From attention to memory in the older adult and Alzheimer's Disease: An integrative suggestion. *International Journal of Psychology and Neuroscience, 1* (1), 219-244.
Received: 24/Feb/2015**; Revised:** 05/May/2015**; Accepted:** 26/May/2015**; Published online:** 17/Jun/2015 **ISSN 2183-5829**