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Type of memory and emotional valence in healthy aging, mild cognitive impairment, and Alzheimer's disease

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Abstract

Background: Autobiographical memory (AM) presents components related to the type of memory and may present an associated emotional valence. Comparing healthy older adults, adults with mild cognitive impairment (MCI), and adults with Alzheimer´s disease (AD) gives contradictory results. We examined AM in these groups to analyze differences and provide information that would contribute to the understanding of AM and associated emotional deficits in patients. **Method:** 31 AD, 32 MCI, and 32 healthy older adults were evaluated using the Autobiographical Memory Test. Taking the number of memories elicited in each category as a dependent variable, an ANOVA of three groups × 3 types of valence was applied (positive, negative, neutral, intrasubject), and another ANOVA of 3 groups × 3 types of memory (specific, general, vague, intrasubject). **Results:** Specific-type responses are reduced with the progression of the pathology and in addition healthy subjects have a positive valence while AD presents a mainly neutral valence. **Conclusions:** Cognitive problems associated with aging tend to affect the highest level of AM specificity. Healthy subjects and MCI have memories with an emotional valence, whereas the AD group has a significant deterioration in these memories.

Keywords: Autobiographical memory, type of memory, emotional valence, mild cognitive impairment, Alzheimer's disease.

Resumen

Tipo de memoria y valencia emocional en adultos mayores sanos, deterioro cognitivo leve y enfermedad de Alzheimer. **Antecedentes:** la memoria autobiográfica (MA) presenta componentes relacionados con el tipo de recuerdo y una valencia emocional asociada a este. Los resultados al comparar adultos mayores sanos, deterioro cognitivo leve (DCL) y enfermedad de Alzheimer (EA) son contradictorios. Se evaluó la MA de estos grupos para analizar diferencias y ofrecer información que contribuya a la comprensión de la MA y los déficits emocionales asociados a los pacientes. **Método:** 31 AD, 32 MCI y 32 adultos mayores sanos fueron evaluados con el Test de Memoria Autobiográfica. Tomando como variable dependiente el número de memorias elicitadas en cada categoría se aplicó un ANOVA de tres grupos × 3 tipos de valencia (positiva, negativa, neutra; intrasujeto), y otro ANOVA de 3 grupos × 3 tipos de recuerdo (específico, general, vago; intrasujeto). **Resultados:** las respuestas específicas se reducen con la progresión de la patología y los sanos presentan mayor recuerdo positivo y los EA principalmente valencias neutras. **Conclusiones:** los problemas cognitivos asociados con el envejecimiento tienden a afectar el nivel más alto de especificidad de la MA. Los sujetos sanos y DCL presentan recuerdos con valencia emocional, mientras que los EA tiene un deterioro significativo en los recuerdos y su asociación a las emociones.

Palabras clave: memoria autobiográfica, tipo de memoria, valencia emocional, deterioro cognitivo leve, enfermedad de Alzheimer.

Autobiographical memory (AM) refers to memories from one's past that are characterized by a sense of subjective time and autonoetic consciousness (Tulving, 2002), which involves a feeling of re-experiencing or reliving the past (Seidl, Lueken, Thomann, Geider, & Schröder, 2011). In contrast to simple episodic recall, autobiographical memory is rich in thoughts, emotions, and evaluations about what happened, and it provides explanatory frameworks that contain human intentions and motivations (Fivush, Habermas, Waters, & Zaman, 2011).

AM contains knowledge with varying levels of specificity, ranging from general knowledge about one's past to highly contextualized-specific knowledge (Conway, 2005). More specifically, AM is composed of two main components, semantic and episodic. The semantic component refers to our knowledge about the world and includes generic information that is probably acquired in many different contexts and can be used in many different situations; semantic AM refers to general responses not linked to particular moments and places; these generic representations cover long periods of a person's life (for example, "when I was studying at the university") and general events referring to thematic events that occur repeatedly (for example, "I used to walk with my dog every afternoon"). Semantic autobiographical knowledge triggers a state of noetic consciousness by which awareness of the past is limited to feelings of knowing or familiarity (El Haj, Antoine, Nandrino, & Kapogiannis, 2015). The episodic component refers to the capacity to recollect individual events, and the essence of this type of memory is its specificity, that is, its capacity to represent a specific event and locate it in time and space; also, autobiographical memory further includes memory of the self as

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the experiencer of the event (autonoetic consciousness), and links past events together into a personal history, essentially forming a life narrative (Fivush, 2011). Episodic AM declines with age and remoteness, whereas the personal semantic nature persists (Piolino, Desgranges, Benali, & Eustache, 2002). Compared to younger adults, healthy older adults are impaired in retrieving episodic contextual details, but age effects are reduced or non-existent in the case of general semantic knowledge (Meléndez, Agusti, Satorres, & Pitarque, 2018).

Cognitive aging research indicates age-related deficits in episodic AM, whereas semantic AM is unimpaired in healthy older adults. However, it is unclear how certain cognitive pathologies such as mild cognitive impairment (MCI) and Alzheimer's disease (AD) affect AM. Older adults' responses to subjective emotional valences are similar to those of young adults (Denburg, Buchanan, Tranel, & Adolphs, 2003), although older adults present a positivity bias in processing emotional stimuli (Carstensen & Mikels, 2005). By contrast, studies considering patients with MCI or AD have revealed uncertain results.

Results with MCI subjects have shown contradictory findings. Compared to healthy adults, numerous studies have shown impairments in the episodic and semantic components, with more significant losses in episodic memory (Irish, Lawlor, O'Mara, & Coen, 2010). Other studies point to losses in the episodic component, whereas the semantic component remains relatively intact (Barnabe, Whitehead, Pilon, Arsenault-Lapierre, & Chertkow, 2012), however, Murphy, Troyer, Levine and Moscovitch (2008) did not detect any deterioration on semantic AM in MCI. Leyhe, Müller, Milian, Eschweiler and Saur (2009) reported that the MCI differed significantly from HC subjects only for recent semantic memory. Two hypotheses arise from these contradictory results: while for Murphy et al. (2008) there is no deterioration because the semantic memory is not linked to a context and therefore does not depend on the hippocampus, on the contrary for Leyhe et al (2010) it can be hypothesized that the time of diminution of AM could mark the beginning of functional impairment in the medial temporal lobe. Regarding research involving subjects with dementia, Seidl et al. (2011) investigated the relationship between semantic and episodic AM, showing that episodic memories deteriorate rapidly in AD, whereas semantic memories are preserved until moderate stages. This conclusion is supported by numerous studies (Piolino et al., 2002; Seild et al., 2011). AD-related autobiographical impairment can be also the consequence of impaired attention and executive dysfunction affecting cognitive control and memory search strategies (El Haj et al., 2015).

Research indicates that when emotional information is compared to neutral stimuli, people pay more attention and have better memory for information with an emotional valence. The meta-analysis by Murphy and Isaacowitz (2008) found that both older and younger adults showed evidence of an emotion salience effect, suggesting that emotional information is processed with greater relevance than neutral information. In addition, some studies have documented an age-related "positivity effect" (Carstensen & Mikels, 2005), where older adults show a preference for positive stimuli over negative stimuli on attention and memory. Moreover, older adults recalled more positive words than negative or neutral words on memory tasks (Charles, Mather, & Carstensen, 2003). Numerous studies have suggested that emotional enhancement of memory relies on several cerebral structures, especially the amygdala (Talmi, Anderson, Riggs, Caplan, & Moscovitch, 2008), and it modulates the hippocampal long-term memory consolidation processes (Vuilleumier, Richardson, Armony, Diver, & Dolan, 2004). During healthy aging, the volume of the amygdala remains relatively intact (Good et al., 2001).

The limited research on emotional memory in MCI has provided disparate findings, and it is difficult to draw conclusions about the extent of the impairment or preservation of emotional memory ability in MCI based on the existing literature (Waring, Dimsdale-Zucker, Flannery, Budson, & Kensinger, 2017). Callahan et al. (2016) found that aMCI patients showed a memory benefit for positive than negative or neutral words, but Parra et al. (2013) found no memory enhancement for emotional material compared to neutral material. Moreover, some studies indicate that patients with AD retain very little neutral (McKhann et al., 2011) or emotional information (Klein-Koerkamp, Baciu, & Hot, 2012), whereas other research indicates that even individuals with AD benefit modestly from emotional memory enhancement (Kensinger, Brierley, Medford, Growdon, & Corkin, 2002). One explanation for these inconsistencies include variability in the stimuli used between studies (words, sentences…) and also the experimental procedure that plays a role in the performance. According to Callahan et al. (2016), emotionally salient information remains especially accessible as the memory trace fades with time and this emotionally-mediated memory consolidation effect over time is also present in patients with memory impairments. This salience would reduce the use of cognitive resources, according to Bahk and Choi (2017), emotional cues make retrieval of AM easier because the retrieval of emotional memories requires less cognitive effort compared to neutral memories. The lighter cognitive load allows cognitive resources to be allocated to regulate or re-interpret affective responses to emotional stimuli, which has been shown to account for emotional enhancement effects in older adults (Leclerc & Kensinger, 2011). Also, Kensinger and Corkin (2003), points out that another possibility is that emotion serves as a unifying theme to memories, allowing items to be more easily clustered as individuals encode the information. Since emotional information is categorically related, it is likely that this factor is often a contributor to the enhancement effect.

This study aimed to compare healthy older adults (HOA) and patients with MCI and AD on the type of AM and its emotional component, in order to identify differences between the groups. Participants responded to the Autobiographical Memory Test (AMT; Williams & Broadbent, 1986) in which they had to elicit a specific memory for each of ten cue words (five of negative valence and five of positive valence). Subsequently, two independent judges determined whether each of these memories had a positive, negative or neutral valence, or was a specific, general or neutral memory. Therefore, considering the contradictory previous results, this study may contribute to better understanding autobiographical memory and the emotional deficits that can be found in MCI and AD patients.

Method

Participants

Thirty-one patients with moderate AD, 32 patients with MCI, and 32 HOA participants matched on age and education took part in the present study (see Table 1 for sociodemographic data). The study was approved by the local ethics committee and conducted according to the ethical standards established in the Helsinki Declaration. Prior to taking part in the study, the participants or their legal representative gave their written, informed consent.

The general inclusion criteria for the study were: age > 65 and no: significant asymptomatic neurovascular disease, a history of previous symptomatic stroke, medical condition significantly affecting the brain, motor-sensory defects, alcohol or drug abuse/dependence, serious psychiatric symptoms, or depressive symptomatology. Patients in the aMCI group met the diagnostic criteria specified by Petersen (2004), and had levels 2 and 3 on the Global Deterioration Scale (GDS) (Reisberg, Ferris, de Leon, & Crook, 1982). The inclusion criteria for AD were: diagnosis of AD determined by the DSM-V (APA, 2013) and had levels 3 and 4 on the GDS (Reisberg et al., 1982). The healthy older participants were recruited from various senior citizen centers in the city of Valencia. All patients were recruited through the Neurology Department at the General Hospital in Valencia, Spain. Clinical diagnosis was the end-result of an extensive evaluation, including medical history and neuropsychological examinations and it was determined through consensus between neurologists and a neuropsychologist (see Table 1 for neuropsychological data).

Instruments

Participants underwent a neurological and neuropsychological assessment. The assessment included GDS (Reisberg et al., 1982), CES-D Depression Scale (Radloff, 1997), and general cognitive functioning: Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), Categorical and Phonological Verbal Fluency from the Barcelona Test Revised (TBR; Peña-Casanova, 2005), Spanish Verbal Learning Test (TAVEC immediate and delayed; Benedet & Alejandre, 1998), Digit Span Forward and Backward subtest of the WAIS-III (Wechsler, 2001), and Copy and Reproduction of Complex Geometric Figures from Rey's Memory Test (Rey, 1999).

Table 1
Means, SD, and differences between groups on cognitive measures

	a. HOA n= 32)	b. MCI (n= 32)	c. AD (n= 31)	significant differences (p < .05)
Age	74.21 (4.67)	76.50 (5.44)	76.96 (5.10)	a = b = c
Gender (male/female)	14/18	12/20	17/14	a = b = c
Education (1-4 scale)	2.59 (.79)	2.31 (.82)	2.29 (.82)	a = b = c
GDS	1.18 (.39)	2.46 (.56)	3.35 (.601)	a > b > c
CES-D	15.46 (4.89)	16.75 (4.58)	16.96 (5.50)	a = b = c
MMSE	28.40 (1.45)	24.68 (3.22)	19.83 (2.26)	a > b > c
Verbal Fluency Test Categorical	21.96 (5.62)	15.56 (4.07)	9.64 (2.88)	a > b > c
Verbal Fluency Test Phonological	35.09 (8.80)	22.87 (5.32)	14.19 (5.65)	a > b > c
TAVEC immediate	46.81 (10.06)	28.16 (7.58)	16.58 (7.04)	a > b > c
TAVEC delayed	10.40 (2.82)	4.32 (3.59)	1.45 (2.63)	a > b > c
Digit Span Forward Test	7.96 (1.44)	7.68 (1.63)	5.90 (1.35)	(a = b) > c
Digit Span Backward Test	4.81 (2.03)	3.53 (1.29)	2.16 (1.26)	a > b > c
Rey Immediate	34.67 (1.46)	27.28 (8.83)	15.11 (10.92)	a > b > c
Rey Delayed	14.65 (4.95)	6.03 (7.22)	.78 (2.36)	a > b > c

Finally, the test used to measure AM was the Autobiographical Memory Test (AMT; Williams & Broadbent, 1986). This test analyzes the valence and type of AM in response to certain cue/words.

Procedure

The procedure and keywords used to assess AM were based on Ricarte, Latorre and Ros (2013). The definitive list consisted of five cue/words with a positive valence - happiness, friendship, smile, energy, illusion - and five cue words with a negative valence - sadness, failure, illness, worry, guilty. The cue/words were presented in a fixed order, alternating positive and negative. The two lists were counterbalanced across participants. Participants were required to retrieve a specific memory in response to each cue/word. The difference between a specific memory and one that was not (general) was explained to them, and an example was provided to help them understand this difference. The interviews were recorded with a voice recorder for later coding according to two categories: valence and specificity. Valence, taking into account the verbalization of the emotion the subject felt at that moment, was classified as positive, negative, or neutral (if the evoked memory did not express any emotion). Specificity of the memory was categorized as vague when it was lacking in details, general when it did not provide information about the specific period, or specific when it was a very specific, day-long memory, where the participant described what happened, what s/he did and felt, the circumstances, with whom, where, and how it happened. Finally, when there was no response to a cue it was considered an omission. There were 32 omissions: 3 omissions in healthy people, 9 in MCI, and 20 AD. Two independent judges individually assessed the recordings to calculate inter-judge reliability. Inter-judge reliability was calculated separately for the type of valence as well as for the type of recall using Kappa statistic (which in the first case analyzes a contingency table of 2 judge's × 3 types of valence on the number of elicited memories, whereas in the second case analyzes a contingency 2 judge's × 3 types of recall on the number of elicited memories). The Kappa statistic for the type of valence was = .78 ($p < .05$), whereas the Kappa statistic for the type of recall was = .82 ($p < .05$), thus showing in both cases an adequate inter-judge reliability.

Data analysis

Data were analyzed using two mixed ANOVAS: One ANOVA of three groups (between subjects) × 3 types of valence (positive, negative, neutral; within subjects), and another ANOVA of 3 groups × 3 types of memory (specific, general, vague; within subjects), taking in both cases as dependent variable the number of memories elicited in each category. Post hoc simple effects tests plus t tests pairwise comparisons with Bonferroni correction ($p <$ .05) were performed when needed.

Results

Type of memory

A mixed ANOVA was performed with three groups (HOA, MCI, AD, between-subjects) and three types of recall (specific, general, and vague; within-subjects) on the number of memories elicited in each type of memory (over a maximum of 10). The main effects of type of memory ($F(2, 184) = 4.24$, $p = .016$, $\eta^2 = .044$; 1-β= .737) and group ($F(2, 92) = 2.91$, $p = .059$, $\eta^2 = .060$; 1-β= .556), as well as the interaction ($F(4, 184) = 16.20$, $p < .0001$, $\eta^2 = .26$; 1-β= .999), were significant.

Given the significant interaction, we carried out two simple effects tests, one comparing the three groups and another comparing the three types of recall. Regarding the study of each group separately (see Table 2) the simple effect test showed a significant effect of the type of recall in the HOA ($F(2, 91) = 7.36$, $p = .001$, $\eta^2 = .139$), with a greater number of specific responses than general ($p = .033$) and vague ($p < .001$) responses. The MCI group did not obtain significant differences between the three types of response ($F(2, 91) = .098$, $p = .907$, $\eta^2 = .002$). Finally a significant effect of the type of recall was obtained in the AD group ($F(2, 91) = 25.06$, $p < .001$, $\eta^2 = .335$), with a greater number of vague responses ($p < .001$) than general and specific responses.

Regarding the comparison of the type of recall between groups the simple effect test showed significant differences between groups for specific responses ($F(2, 92) = 22.81$, $p < .001$, $\eta^2 = .332$), with a greater number in HOA than in MCI ($p = .010$) and AD ($p < .001$), and a greater number in MCI than in AD ($p = .025$). The simple effect test also showed significant differences between groups for general responses ($F(2, 92) =5.96$, $p = .004$, $\eta^2 = .115$), with a greater number inHOA and MCI than in AD ($p = .021$, $p = .006$). Finally there were also significant differences between groups for vague responses ($F(2, 92) = 19.05$, $p < .001$, $\eta^2 = .293$), with a greater number in AD than in HOA and MCI ($p < .001$).

Valence of the memory

A mixed ANOVA was performed with three groups (between-subjects) and three valences (positive, negative, and neutral; within-subjects) on the number of memories elicited in each type of valence (over a maximum of 10), showing significant main effects for valence ($F(2, 184) = 43.69$, $MSe = 3.22$, $p < .0001$, $\eta^2 = .322$; 1-β= 0.999) and group ($F(2, 92) = 3.33$, $MSe = 0.25$, $p = .04$, $\eta^2 = .067$; 1-β = .616), as wells as their interaction ($F(4, 184) = 8.85$, $MSe = 3.22$, $p < .0001$, $\eta^2 = .161$; 1-β = .999).

Given the significant interaction, we carried out two simple effects tests, one comparing the three groups and another comparing the three types of valence (see Table 3). Regarding the study of each group separately the simple effect test showed a significant effect of the valence in HOA group ($F(2, 91) = 30.28$, $p < .001$, $\eta^2 = .400$) and in the MCI group ($F(2, 91) = 18.69$, $p < .001$, $\eta^2 = .291$), with a greater number of positive and negative responses than neutral ones ($p < .001$). The AD group did not show significant differences ($F(2, 91) = .292$, $p = .748$, $\eta^2 = .006$) because its production of memories had similar valences for the three categories.

Table 2
Means of number of elicited memories (SD) according to the type of response

	Specific	General	Vague
Healthy older adults	4.53(2.18)	3.13(2.02)	2.25(1.45)
MCI	3.09(1.87)	3.31(1.55)	3.31(1.90)
AD	1.80(1.58)	1.90(1.64)	5.67(2.65)

Table 3
Means of number of elicited memories (SD) according to the valence

	Positive	Negative	Neutral
Healthy older adults	4.15(1.09)	4.70(1.39)	1.07(.98)
MCI	3.97(1.23)	4.28(1.51)	1.47(1.45)
AD	3.29(1.50)	3.13(1.35)	2.94(2.44)

Regarding the comparison of the valences between groups the simple effect test showed significant differences between groups for positive responses ($F(2, 92) = 3.71$, $p = .028$, $\eta^2 = .075$), with a greater number in HOA than in AD ($p = .035$). The simple effect test also showed significant differences between groups for negative responses ($F(2, 92) = 10.44$, $p < .001$, $\eta^2 = .185$), with a greater number in HOA and MCI than in AD ($p < .001$, $p = .005$). Finally the simple effect test also showed significant differences between groups for neutral responses ($F(2, 92) = 10.15$, $p < .001$, $\eta^2 = .181$), with a greater number in AD than in healthy older adults and MCI ($p < .001$, $p = .003$).

Discussion

The present study investigated whether normal aging, MCI, and AD affected the type of memory and the valence of this memory. A reduction in specific memories as the cognitive pathology advanced was verified, making access to autobiographical memories difficult at the highest levels of cognitive pathology. In addition, in subjects with AD, a deterioration in memories linked to emotional responses was observed.

Regarding the type of memory, our results are consistent with the common observation that the impairment in MCI lies between that of normal aging and AD. HOA showed a significantly greater number of specific memories than general and vague memories; when this type of response is compared to the other two groups, significant differences are observed, suggesting that cognitive problems associated with aging tend to affect the highest level of AM specificity. In the MCI group, no differences between the three types of responses were obtained. As Murphy et al. (2008) concluded, in MCI, episodic memory, compared to personal semantic memory, is probably disproportionately affected by hippocampal damage. Episodic and semantic autobiographical memories are differentially affected by the early brain changes associated with MCI, with a significantly greater reduction in episodic content than in semantic content (general memories). This conclusion would be reinforced by the result indicating that, between the group of HOA and the MCI patients, there were no differences in general memories, although both groups obtained significantly higher numbers than the subjects with AD. Finally, AD patients have a significantly higher number of vague responses due to memory deterioration with the progression of the disease. Autobiographical recall in AD is mainly characterized by a substantial loss of episodic information, leading to a decontextualization of autobiographical memories and a shift from mentally reliving past events to a general sense of familiarity. This decline is exacerbated by anterograde and retrograde amnesia. McClelland, McNaughton and O' Reilly (1995) argued that the hippocampal formation is critical to the consolidation of memories, but once memories are consolidated they become represented in neocortical areas and their retrieval then becomes independent of hippocampal networks. Multiple Trace Theory (Nadel, Winocur, Ryan, & Moscovitch, 2007) proposes that, unlike episodic memory, personal semantic memory becomes independent of the medial temporal lobe over time. By this view, semantic memories are transferred over time to the neocortex and the mediotemporal structures are no longer necessary for their retrieval, whereas retrieval of episodic memories is always dependent on the interaction between hippocampus and neocortex. Hence, the model predicts that semantic AM are likely to be less affected by the pathological mechanisms of AD compared to episodic AM (El Haj et al., 2015).

The results for the valence responses reveal that HOA and MCI, when presented with stimuli, mainly evoke memories with emotional content (positive and negative), whereas in the AD group, there were no differences between the number of memories evoked with and without an emotional valence. As Broster, Blonder and Jiang (2012) point out, there is a strong behavioral basis for the belief that emotional content might improve memory outcomes, even in older adults. Our results showed that this finding was also observed in subjects with MCI. Thus, the amygdala in MCI subjects may not be sufficiently deteriorated yet to diminish emotional responses. A pathological study (Braak, Griffing, Arai, Bohl, Bratzke, & Braak, 1999) has shown that neurodegeneration in AD begins in the medial temporal lobe (including the hippocampus, amygdala, and parahippocampal gyrus), and the modified tissue density in the amygdala has been used as a feature in AD and MCI discrimination (Ewers et al., 2012). As stated above, in AD, there are two opposite hypotheses. Whereas some studies indicate that they do not appear to benefit from emotional enhancement, other studies indicate that even individuals with AD benefit modestly from emotional memory enhancement. The results confirm the first hypothesis, without observing a greater number of memories with an emotional valence. In addition, when the three groups were compared, the AD subjects had significantly more non-valence responses than the healthy subjects and the MCI. The volume of the amygdala shrinks in AD, and this atrophy is pronounced, even in the early stages of the disease (Keisinger et al., 2002).

The comparison of the groups based on the emotional valence of the response indicates the existence of a positivity effect in the HOA compared to the AD group, possibly due to the reduction in responses with emotional content that occurs in the group with dementia. As Broster et al. (2012) point out, AD patients do not appear to benefit from emotional memory enhancement in the processing of complex information such as verbally related stories. In addition, in the negative valence responses, both the HOA and the MCI showed differences from the AD group. These results are consistent with those obtained by Kensinger et al. (2002), who showed that AD patients present an impairment in the emotional enhancement of memory on a recall task for both negative and positive pictures, negative and positive words, and negative sentences. Budson et al. (2006) concluded that the deterioration of the amygdala present in AD disrupts the way this structure influences the subjective feeling about information that has been seen before, making its recall difficult. Thus, the preference for memory of one emotional type has been shown to be minimized in subjects with AD.

Finally, it is important to note that the current findings are specific to cue stimuli, which can make it difficult to compare our results to previous findings reported in the literature that are often based on other evaluation techniques such as Autobiographical Memory Interview (Kopelman, Wilson, & Baddeley, 1990).

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