A comparison of memory and executive functions in Alzheimer disease and the frontal variant of frontotemporal dementia

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This study examined memory and executive functions of switching and distributing attention in 25 Alzheimer patients (AD), 9 patients with frontal variant of frontotemporal dementia (fvFTD), and 25 healthy older people, as a control group, in three tasks: verbal digit span, Brown-Peterson (B-P) task, and dual-task. No differences were found in digit span. Qualitative analysis of errors in the B-P task indicated that both ADs and fvFTDs presented a higher number of omissions and perseverations, interpreted in this study as an index of executive dysfunction, compared to the control group. In fact, the ADs persevered more or the same as the fvFTDs, and no differences were found between the two groups of patients in omissions. The dual-task results showed that both AD and fvFTD had difficulties coordinating the two tasks simultaneously compared to the control group, but no differences were found between the patient groups. Although the presence of alterations in the executive functions of AD patients may suggest that these functions would depend on the correct functional integration of various cerebral areas, it would be of great interest to include neurological evidence in order to contrast these results in future research.

Comparación entre memoria y funciones ejecutivas en la enfermedad de Alzheimer y la variante frontal de la demencia frontotemporal. Este estudio examinó la memoria y las funciones ejecutivas de cambiar y distribuir la atención en 25 pacientes Alzheimer (EA), 9 pacientes con demencia frontotemporal en su variante frontal (DFTvf), y 25 ancianos sanos, como grupo control (C), en tres pruebas: amplitud verbal, tarea de Brown-Peterson (B-P), y una tarea doble. No se encontraron diferencias significativas en amplitud. El análisis de los errores de la tarea B-P indicó que tanto los EA como los DFTvf presentaban mayor número de omisiones y perseveraciones que C, interpretándose ambos errores como un índice de disfunción ejecutiva. Además, los EA perseveraron más o igual que los DFTvf y no se encontraron diferencias significativas entre ambos grupos de pacientes en omisiones. En la tarea doble, tanto los EA como los DFTvf tuvieron dificultades para coordinar ambas tareas simultáneamente, comparado con C, pero no se encontraron diferencias significativas entre EA y DFTvf. Si bien la presencia de alteraciones de las funciones ejecutivas en pacientes EA, podría sugerir que estas funciones dependerían de la correcta integración funcional de varias áreas cerebrales, sería de gran interés incluir evidencia neurológica en investigaciones futuras, para contrastar estos resultados.

In the last few years, there has been increasing interest to examine the executive functions (Stuss & Alexander, 2000; 2005) in patients who have suffered diverse types of brain damages, as well as in patients with neurodegenerative illnesses such as frontal variant of frontotemporal dementia (fvFTD), or Alzheimer's disease (AD). There is high consensus among diverse authors (Lund & Manchester Groups, 1994; Neary, Snowdown, Gustafson, et al., 1998) to consider that fvFTD patients, according to diagnostic criteria, suffer an important deterioration of the executive functions (see the review of Grossman, 2002). They present a «dysexecutive syndrome», characterized by behavioral and cognitive disorders

mainly related to the central executive, according to the working memory model of Baddeley (1986), as well as to action planning, or problem solving, among others. In fact, from the neuroanatomical viewpoint, frontotemporal damages such as the presence of atrophy and anterior frontotemporal hypoperfusion have been observed in fvFTD patients (McKhann, Albert, Grossman, Miller, Dickson, & Trojanowski, 2001). Various frontal dysfunctions, such as perseveration, difficulty to change strategies or to inhibit responses, have been examined with different tasks (Wisconsin, Stroop, the A and B Trail Making or the Go/No Go Test; see Collette, Amieva, Adam, et al., 2007).

In AD, the brain damages observed are more diffuse than in fvFTDs, presenting a global pattern of neocortical atrophy with biparieto-temporal and limbic predominance that lead to a syndrome characterized by aphasia, apraxia and agnosia along with diverse psychopathological changes. However, although the presence of visoconstructive problems and memory impairment can facilitate the differential diagnosis with fvFTD (Giovagnoli,

Fecha recepción: 7-5-09 • Fecha aceptación: 14-9-09 Correspondencia: María Victoria Sebastián Gascón Facultad de Psicología Universidad Complutense de Madrid 28223 Madrid (Spain) e-mail: mysebastian@psi.ucm.es Erbetta, Reati, & Bugiani, 2008), executive dysfunctions have now also been observed in AD patients. Thus, in recent years, various studies (for example, MacPherson, Della Sala, Logie, & Wilcock, 2007; see also Baddeley, Eysenck, & Anderson, 2009) have shown that AD patients also display difficulties in distributing attention between tasks, inhibitory control and switching attention, in first stages of the illness

Some studies have compared the performance of these two types of patients in memory tasks and executive tasks, showing that ADs present poorer recall in memory tasks than fvFTDs and, in contrast, the latter perform worse in executive tasks, but other studies have indicated memory problems (i.e., low digit span) in fvFTD patients too (Grossman, 2002).

The Brown-Peterson (B-P) task has been a classic procedure in memory research to assess short-term memory. It consists of presenting series of three consonants to participants and asking them to remember them in the same order in which they were presented. To prevent participants from rehearsing, they are asked to count backwards before the recall. This information must be inhibited by the subjects in order to remember the consonants correctly and, therefore, ADs' poor performance in this task has been interpreted by various authors (for example, Belleville, Peretz & Malenfant, 1996), as executive dysfunctions, specifically, in the central executive, following Baddeley's working model. Upon analysing the errors committed by ADs and a control group of healthy older people in the B-P task, some studies showed (Dannenbaum, Parkinson, & Inman, 1988; Kopelman, 1985) that omissions predominated in ADs, indicating that the information had not been encoded, whereas the distribution of errors was more homogeneous in controls. However, Sebastian, Menor and Elosua (2001), found that the ADs mainly committed a large number of perseverations and they interpreted those in terms of executive problems, that is, the ADs could not switch their attention to the following item presented, and their attention remained «anchored» in the previously remembered item. These perseverations have been found in patients with executive dysfunctions and, as noted by Stuss and Alexander (2005), they indicate a «supervision» or «monitoring» deficit. However, this B-P task has not been used in fvFTD patients and, therefore, the errors committed by these patients have not been examined. In contrast, some authors (Grossman, 2002) have observed that one of the aspects that discriminates these two types of dementia is perseverative behaviour, that is, fvFTDs commit more perseverations than ADs in tests like the Wisconsin Test.

Another of the executive functions examined has been the capacity to coordinate and distribute attention between two tasks. For this purpose, Della Sala, Baddeley, Papagno and Spinnler (1995) designed a dual-task procedure that has been extensively used with AD patients (for example, MacPherson, et al., 2007; Sebastian, Menor, & Elosua, 2006) and that consists of presenting a tracking task and a digit sequence recall task simultaneously, so that participants have to recall series of digits previously given at their own span, while they must put crosses in boxes as fast as possible. The data showed that the ADs had problems switching their attention between the two tasks, in comparison to the elderly control. This dual task has not been used to examine fvFTD patients, but Giovagnoli et al. (2008) carried out a study aimed at comparing diverse cognitive functions of ADs and fvFTDs. They assessed cognitive flexibility, that is, the capacity to switch attention from one group to another. For this purpose, they used

tasks like the Trail Making Test B and the Weigl Sorting Test, finding no significant differences between ADs and fvFTDs.

The general goal of the present study is to examine memory and executive functions (switching and distribution attention) in patients fvFTD and AD, and in elderly control, and to compare the performance of both groups of patients in three tasks: verbal digit span, B-P task, and dual-task. More specifically, to check whether the fvFTD patients' performance in these memory tasks (digit span and B-P) is better than that of the AD patients, in terms of span and errors.

A second goal is to analyse the errors committed in the B-P task, and determine whether the fvFTDs have the same pattern of errors as the ADs and/or whether they commit the same number of omission and perseveration errors. Because of AD's encoding problems, these would be expected to present a higher proportion of omissions when compared to controls and fvFTDs. Considering perseverations as an index of executive dysfunctions, if the fvFTD persevere more, they would show a higher proportion in the number of consecutive repetitions when compared to controls and ADs. The third goal was to examine performance in the dual-task, and verify whether the fvFTDs have more difficulties than the ADs to coordinate and distribute attention.

Method

Participants

In this study, there are 59 participants: 25 outpatients Alzheimer (AD), 7 males and 18 females, diagnosed as probable Alzheimer by the neurology team of a clinical centre of Madrid, and presenting a mild degree of severity according to NINCDS/ADRDA criteria (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984), with a mean age of 73.48 years (SD=4.39, range=65-82), a mean of 7.76 years of education (SD= 2.91, range= 6-14), and a mean MMSE (Folstein, Folstein, & McHugh, 1975) of 20.36 (SD= 2.18, range= 16-23) and a median of 20; 9 outpatients with frontotemporal dementia (fvFTD), 5 males and 4 females, diagnosed by the neurology team of another clinical centre of Madrid, according to Lund and Manchester Groups (1994) criteria, and presenting fvFTD's characteristics of Neary et al.'s typology (1998), with a mean age of 65.22 years (SD= 6.59, range= 53-73), a mean of 15.67 years of education (SD= 3.39, range= 8-19), and a mean MMSE of 26.67 (SD= 2.23, range= 22-29), and a median of 27; and 25 healthy older people as a control group (C), 6 males and 19 females, from a Day Centre of Madrid, with a mean age of 72.72 years (SD= 4.59, range= 65-82), and a mean of 7.12 years of education (SD= 1.74, range= 6-14), and a mean MMSE of 27.68 (SD= 2.14, range= 24-30), and a median of 29. Some of the AD patients and controls had participated in other studies (Sebastian et al., 2001, 2006), and their scores in the MMSE remained constant from 2005 to 2006, year in which this study was carried out. Neither of the participants suffered psychiatric disorders nor physical handicaps.

The fvFTD group was younger and had more years of education than the AD group (age [U= 28, Z= -3.31, P<.001]; education level [U= 11, Z= -4.18, P<.0001]), and C (age [U= 38.5, Z= -2.90, P<.004]; education level [U= 7, Z= -4.35, P<.0001]).

Materials and procedure

The tasks were administered individually to all participants and the following order was used: (a) memory span task, (b) B-P

task, (c) 15 minutes rest, (d) single-condition box-crossing task, (e) digit sequences recall, (f) 15 minutes rest, and (g) dual-task, box-crossing and digit sequences recall simultaneously. The participant sat in front of the researcher.

Memory Span

It consists of repeating series of digits, read aloud by the experimenter at a rate of one per second. The task began with three series of three digits and the length of the sequence increased by one as the test proceeded. The participant is requested to remember them immediately in the same order as they were pronounced. The longest sequence that the participant could recall correctly in two out of the three series was considered the participant's memory span.

B-P Task

The material of the B-P task differed from the original (see Badeley et al., 2009), but it had been used in a previous study (Sebastián et al., 2001). It consisted of presenting 21 randomly selected two upper-case consonants, appearing in the centre of a white spiral-bound 10×15 -cm card. These were placed on the table so participants could read them clearly. Participants were asked to read the two consonants and were informed that they would have to remember them later in the same order as they had been presented. There were three experimental conditions: retention interval of 7, 14, and 21s. Once the participants had read the consonants, they had to turn the card over. Next, a number was said and they were asked to begin to count forwards, one-by-one, from that number. After the previously fixed time interval, they were asked to remember the consonants in the same order as they had been presented.

Tracking Task

The tracking task was a pencil-and-paper test designed by Della Sala et al. (1995), consisting of 80 boxes linked in a chain. Participants were asked to begin at one end of the chain and to draw a cross on each square as fast as possible, for 2 min. Additional pages were given, if necessary, to reach time limit. This task was carried out both in single and dual conditions.

Digit Sequence Recall

The material for the sequences of digits in single and dual conditions consisted of series of digits related to the participant's memory span, read to the participants during 2 minutes.

Dual-Task

Participants simultaneously performed the tracking task and the digit recall for 2 min.

Statistical analyses

As the data do not fulfill the ANCOVAs assumptions, the nonparametric Mann–Whitney test was carried out to analyse intergroup differences in memory span, errors in B-P and dual tasks. To take into account the age and education differences between AD and fvFTD patients, and between fvFTD and Control group,

covariance analyses were also performed with age and education as confounding variables.

Results

As in other studies (for example, Collette et al., 2007), the results were analysed by comparing, on the one hand, the performance of each group of patients to the control group in each task, to determine the generality or specificity of memory and executive functions in each pathology; on the other hand, the performance of the two groups of patients were compared to each other in each task to determine whether the pattern of deficit of executive functions was similar in both types of dementia.

Neither age nor education resulted as significant predictors in any analysis (p>.05). For this reason, as the ANCOVAs results were consistent to those obtained with the Mann-Whitney nonparametric test, 2-tails, only M-W's will be reported.

Memory Span Task

The three groups of participants had a similar verbal digit span (AD, M= 4.20, SD= 0.65; fvFTD, M= 4.22, SD= 0.83; C, M= 4.44, SD= 0.76). Neither of the comparisons revealed significant differences between each group of patients and the control group (P>.05), nor between AD and fvFTD (P>.05).

Errors in The B-P Task

The results were corrected as a function of errors committed by all participants. Of the total errors made (confusions, perseverations, omissions, and order alterations) in the three intervals, this study has taken into account omissions and perseverations. In order to compare the groups, the proportions of total omissions and perseverations committed by the participants were computed. In the case of 0 or 1 values, Bartlett's suggestion was followed (cited by Kirk, 1982. That is, if p=1 [$p=1-\frac{1}{2}$ n]; if p=0 [$p=\frac{1}{2}$ n]).

Omissions

When the participant did not remember either the first or second letter presented, or did not remember any of them (this would be a blank response), an omission was committed (Table 1). Significant

Table 1 Mean proportions (standard deviations in parenthesis) of errors in the B-P task committed by group											
	Omis- sions	One- letter perseveration			Two-letter perseveration						
Group		Once	Twice	than 3 times	Once	Twice	+ than 3 times				
AD	.11	.56	.26	.20	.61	.09	.09				
	(.11)	(.31)	(.27)	(.24)	(.42)	(.14)	(.18)				
fvFTD	.21	.62	.09	.06	.52	.09	.06				
	(.18)	(.43)	(.09)	(.01)	(.44)	(.09)	(.01)				
С	.09	.61	.04	.03	.20	.03	.02				
	(.21)	(.46)	(.07)	(05)	(.37)	(.06)	(.01)				

differences were found in the comparison of each group of patients with the control group (AD, M= 0.11; C, M= 0.09 [U= 207, Z= -2.35, P<.01] (fvFTD, M= 0.21; C, M= 0.09 [U= 30.5, Z= -3.59, P<.0001], but ADs and fvFTDs had a similar number (P>.05).

Perseverations

Perseveration was considered when the participant repeated the response given in the immediately preceding trial. The total perseveration proportions were computed according to whether they were of one or two letters and these were subdivided according to the number of times they were repeated consecutively, resulting in three types (once, twice, or more than three times). No differences were found in one-letter perseverations repeated once (Table 1). Significant results were observed in one-letter perseverations repeated twice or more than three times. ADs and fvFTDs committed more perseverations of this kind when compared to Controls (repeated twice, AD, M = 0.26; C, M = 0.04; [U= 110, Z= -4.44, P<.0001]; fvFTD, M= 0.09; C, M= 0.04 [U= 17, Z= -4.53, P<.0001]; repeated more than three times, AD, M=0.20; C, M=0.03 [U= 173.5, Z= -3.50, P < .0001]; fvFTD, M = 0.06; C, M = 0.03[U= 9, Z= -5.09, P<.0001], but both patients did not differ from each other (P>.05).

Referring to two-letter perseverations (see Table 1), the analysis indicated that both patients committed more two-letter perseverations repeated once than Controls (AD, M=0.61; C, M = 0.20 [U= 147.5, Z= -3.52, P < .0001]; fvFTD, M = 0.52; C, M = 0.20; [U = 40, Z = -3.18, P < .001], but AD and fvFTD had a similar number of two-letter perseverations repeated once (P>.05). However, with regard to two-letter perseverations repeated twice, and more than three times, all the comparisons were significant, both AD and fvFTD had more errors of these kind than Controls (repeated twice, AD, M= 0.09; C, M= 0.03 [U= 59, Z= -2.28, P < .02]; fvFTD, M = 0.09; C, M = 0.03 [U= 9, Z= -5.07, P < .0001]; repeated more than three times, AD, M = 0.09; C, M = 0.02 [U= 262.5, Z= -2.06, P<.03]; fvFTD, M= 0.06; C, M= 0.02 [U= 325, Z=-5.75, P<.0001); and ADs committed more two-letter perseverations repeated twice ([U= 59, Z= -2.28, P<.02], and repeated more than three times [U= 36, Z= -3.46, P<.001]) than fvDFTs.

Tracking Tasks and Digit Sequence Recall in Single and Dual Conditions

In relation to the Tracking Task (Table 2), the total number of crosses made during 2 min. was the participant's score in single and dual conditions. The same pattern of results was found in the single and dual conditions. ADs put less crosses (single condition, M=68.20; dual condition, M=57.92, respectively) than Cs (single condition, M=109.64 [U= 104.Z=-4.05, P<.0001], dual condition, M=98.44 [U= 115.5, Z=-3.82, P<.0001]), and fvDFTs (single condition, M=111.78 [U= 44.5, Z=-2.66, P<.008], dual condition, M=92.56 [U= 53, Z=-2.32, P<.02]), but no significant differences were found between fvDFT and Control in the single (P>.05) or in the dual condition (P>.05).

With respect to the digit sequence recall task (Table 2), correct recall was considered the proportion of series correctly remembered in this 2-min interval in single and dual conditions. As expected, no significant differences were found in the single condition in any of the comparisons (AD, M= 0.83; C, M= 0.77;

fvDFT, M= 0.77, (P>.05). However, the pattern of results changed in the dual condition (Table 2): ADs remembered correctly fewer series of digits (M = 0.61) than Cs (M= 0.76 [U= 213, Z= -1.93, P<.05]). But, the fvFTDs (M= 0.70) differed significantly neither from Controls (P>.05) nor from ADs (P>.05).

According to Baddeley (see Baddeley et al., 2009), it was computed both the losses in the tracking task and in the digit sequence recall in the dual condition as well as the distribution of attention between the two tasks in the three comparisons carried out (Table 2). The proportional loss of crosses in the dual condition was similar in the three groups (AD, M = 0.17; C, M = 0.10; fvFTD, M=0.17), not finding any significant difference (P>.05). On the other hand, the drop in digit sequence recall in the dual condition (Table 2) was fairly high in ADs (M=0.21) when compared to C (M = 0.006 [U = 162, Z = -2.92 P < .003]), but fvFTDs (M = 0.07)were not different from C (P>.05), nor from the ADs (P>.05). With regard to attention distribution between the two tasks or mu index, the analysis indicated significant differences between each group of patients and the control group (AD, M= 78.61; C, M= 93.15 [U= 162.5, Z= -2.91, P<.004]; fvFTD (M= 87.39 [U= 58.5, Z= -2.11 P<.03], but, in contrast, ADs and fvFTDs did not diverge from each other (P>.05). AD and fvFTD performed more poorly in the distribution of attention between the two tasks than the elderly Control.

Discussion

This study examined memory and executive functions (switching and distribution attention) in AD patients, fvFTD patients, and a control group in three different tasks: digit span, the Brown-Peterson task, and a dual task. In relation to verbal digit span, the three groups had a fairly low span, about four digits, not showing significant differences. This seems to indicate that this effect is more due to age (Baddeley et al., 2009) and the subsequent cognitive ageing than to the type of dementia.

The purpose of analysing the errors in the B-P task was to check whether the two groups of patients had the same pattern of results. Our study showed mostly perseverations. Different authors (for example, Stuss & Alexander, 2005) have considered these perseverations an index of executive dysfunctions and an

Table 2

Mean (standard deviations in parenthesis) of boxes crossed, correct digit sequences recall in the single and dual conditions, pt, pm, and mu indexes by group

Group	Single Crosses	Double Crosses	Single Digits	Double Digits	pt*	pm**	mu***
AD	68.20	57.92	.83	.61	.17	.21	78.61
	(28.0)	(28.7)	(.11)	(.26)	(.21)	(.27)	(20.07)
fvFTD	111.78	92.56	.77	.70	.17	.07	87.39
	(40.91)	(37.75)	(.15)	(.12)	(.17)	(.12)	(7.40)
С	109.64	98.44	.77	.76	.10	.006	93.15
	(33.2)	(33.24)	(.15)	(.13)	(.12)	(.11)	(5.19)

^{*} pt = (tracking in single condition – tracking in dual condition) / tracking in single condition

^{**} pm = recall of sequences of digits in single condition – recall of sequences of digits in dual condition

^{***} mu = (1 - (pm + pt) / 2) * 100

instrument to discriminate fvFTD and AD patients (Grossman, 2002). According to this assumption, the fvFTD patients should persevere more than the ADs. However, in our results, the ADs persevered more or the same as the fvFTD patients, with both groups displaying executive dysfunctions because they were not capable of switching attention or renewing the contents of the working memory, specifically presenting a dysfunction in the central executive or attentional component of Baddeley's working memory model (1986), or a deficit of supervision or monitoring (Stuss & Alexander, 2005).

Although the presence of omissions in memory tasks had been interpreted in other studies (Dannenbaum et al., 1988; Kopelman, 1985), as problems of encoding and, therefore, it had been related to AD patients, it could be explained in similar terms as perseverations, because the B-P task requires the capacity to inhibit information given between the presentation of the letters and the recall, in order to rehearse the letters presented. Our results showed omission errors, not only in AD patients but in fvFTDs too, probably reflecting executive problems, what prevents them from rehearsing.

In relation to the results of the dual-task, both the AD and the fvFTD patients had difficulties to coordinate both tasks simultaneously in comparison to the healthy elderly people, supporting the results and interpretation of other authors about the presence of a dysfunction in the central executive (MacPherson et al., 2007; Baddeley et al., 2009).

As the digit sequences recall is a memory test, it could be criticized that this dual-task was not appropriate to contrast fvFTD and AD patients because it is made up of a task that requires memory. However, it must be taken into account that the data are a function of the span of each participant, and the goal of this dual-task is to observe the patient's capacity to perform the tracking task and the digit sequences recall simultaneously, and so, be able to divide their attention between them, thus, assessing the executive function. On the other hand, it is important to underline that the fvFTD sample is not very large in comparison to the AD group, although the number of clinical cases diagnosed with frontotemporal dementia, in all its four variants, in Spain is around 5000 patients (Pastor's Report, 2006, Navarra's University).

To conclude, the AD patients displayed more memory deterioration than the fvFTD patients, but both groups presented dysfunction of the executive processes of switching and dividing attention. If, as mentioned, fvFTD patients specifically present frontotemporal alterations and, in turn, these are related to executive functions, the fvFTDs would be expected to present difficulties in these tasks, as reported in the diagnostic criteria and in diverse investigations, and, as observed in this study. Moreover,

the fvFTDs would also be expected to present more executive dysfunctions than the ADs, however, the results of this study reflect that these alterations are also present in the ADs, showing a worse capacity to inhibit information and an even higher tendency towards perseveration than fvFTDs, as observed in the B-P task. These results raise several questions. On the one hand, it could be considered the perspective of some authors such as Stuss and Alexander (2000), who defend that the executive functions are not reduced to the prefrontal and dorsolateral cortex, but that their correct functioning depends on the neural connections among diverse brain areas. Jurado and Roselli (2007) consider that the cooperation among the frontal lobes, the limbic system, and posterior areas of the cortex allows one to perform the processes involved in the diverse executive functions. Ultimately, all these authors coincide in considering them, far from being only related to the frontal lobes, to be the result of the correct functional integration of multiple areas of the cerebral cortex (posterior, subcortical, and thalamic paths), which would explain the fact that AD patients, with a diffuse pattern of cerebral atrophy more focused on temporoparietal and limbic areas, also show impairment of the executive system in early stages of the illness. Nevertheless, it may be of interest to include techniques such as diffusion tensor imaging and evoked potentials in order to establish whether the presence of executive dysfunctions in AD reflect dorsolateral prefrontal atrophy, among others, or not, as it can occur in moderate stages of the disease. We should not forget the fact that AD, as it can follow very different ways of progression from one patient to another, it may be altering diverse and different neuropsychological functions, depending on the particular progression of the AD patient, and thereby impairing the performance of certain tasks to a greater extent. Therefore, this study suggests the need to carry out future research taking into account neurological evidence, selecting tasks to verify the differences observed and aimed at the establishment of other differential diagnosis criteria of AD and fvFTD that do not rely on the presence of impairment of executive functions.

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