Greater Relative Impairment of Object Recognition Than of Visuospatial Abilities in Alzheimer’s Disease

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Histological investigation in Alzheimer’s disease (AD) has indicated that the concentration of neurofibrillary tangles in inferotemporal cortex (IT) is greater than that found in posterior parietal cortex (PPC). Researchers hypothesized that the relative degree of impairment of visual function subserved by each of these cortical areas should reflect the disproportionate distribution of neuropathological changes. Eleven AD patients and 16 elderly controls received 8 tests of visual function, 4 of which have been shown previously to be selectively affected by IT lesions and 4 that are selective for PPC lesions. AD patients were significantly impaired on all 8 tests, but multivariate analysis indicated a relatively greater impairment on tests of IT function. The greater impairment of visual function mediated by IT relative to function mediated by PPC is consistent with differential degradation of the respective cortical areas.

Several types of visual impairments are reported to occur in the early and intermediate stages of Alzheimer’s disease (AD; for review, Katz & Rimmer, 1989; Mendez, Tomsak, & Remler, 1990). Unlike memory impairment, which is an obligatory correlate of AD, visual impairments vary in prevalence and severity (Mendola, Cronin-Golomb, Corkin, & Growdon, 1995). Cases range from individuals who are free from any observable dysfunction to those who manifest Balint’s syndrome (Hof, Bouras, Constantinidis, & Morrison, 1989), visual agnosia (Katz & Rimmer, 1989), or simultanagnosia (Trobe & Bauer, 1986). The heterogeneity of visual function likely reflects individual differences in the regional distribution of neuropathological changes. This idea is supported indirectly by positron emission tomography (PET) glucose metabolism studies (Grady et al., 1993) and by direct histological examination of AD brains (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991; Bouras, Hof, Giannakopoulos, Michel, & Morrison, 1994).

The nature and distribution of neuropathological changes in the visual system of AD patients should supply a framework to categorize visual symptoms. One scheme to delineate visual symptoms was based on prefrontal visual channels. Histological examination of the optic nerves of AD patients revealed a reduction in the number of large axon retinal ganglion cells, relative to age-matched controls (Hinton, Sadun, Blanks, & Miller, 1986). The interpretation of this finding was that the magnocellular precortical pathway was selectively vulnerable in AD patients (Bassi & Lehmkuhle, 1990; Hinton et al., 1986; Sadun & Bassi, 1990). However, psychophysical evidence did not support this prediction: Kurylo et al. (1994) showed that AD patients have visual deficits on tests that measure the functional integrity of the magnocellular as well as the parvocellular system. On the basis of these results, they concluded that visual impairment in AD is not limited to functions subserved exclusively by the magnocellular precortical system.

Another approach to understanding visual impairments in AD postulates that the patterns of cortical lesions are likely correlates of visual dysfunction. This view gains support from the study of Rizzo et al. (1992), who found that retinocalcarine function appears to be preserved in AD. Furthermore, primary visual cortex is relatively free of neuropathological change, whereas modality-specific visual cortex and high-order (polymodal) cortices are more vulnerable (Arnold et al., 1991; Hof & Morrison, 1990; Lewis, Campbell, Terry, & Morrison, 1987; Pearson, Esiri, Hiorns, Wilcock, & Powell, 1985). This pattern of pathology suggests a delineation of function according to basic versus higher order visual processing. In many respects, this scheme of segregation appears valid. Basic visual functions such as visual acuity (Katz & Rimmer, 1989) and critical flicker fusion (Cronin-Golomb, Corkin, Rizzo, Cohen, Growdon, & Banks, 1991; Cronin-Golomb, Sugiura, Corkin, & Growdon, 1993) in AD patients are comparable with age-matched controls. However, intermediate levels of visual processing,
including color (Cronin-Golomb et al., 1991), stereoscopic vision (Stevens et al., 1991), motion (Trick & Silverman, 1991), visual grouping (Kurylo, Corkin, & Growdon, 1994), and figure-ground separation (Kurylo et al., 1994; Mendez et al., 1990) are impaired in AD. Furthermore, high-order visual function, including abilities more dependent on cognitive components, such as complex object recognition (Flekkoy, 1976; Mendez et al., 1990), reproducing composite drawings (Flekkoy, 1976), and identifying and locating complex stimuli (Levine, Lee, & Fisher, 1993) are significantly impaired in AD.

In this study, we have extended the cortical hypothesis of visual dysfunction in AD and examined whether impairment of visual function may be segregated on the basis of cortical visual pathways. Visual processing beyond primary visual cortex follows two major cortical streams (Desimone & Ungerleider, 1989; DeYoe & Van Essen, 1988; Livingstone & Hubel, 1987; Maunsell, 1987; Maunsell, Nealey, & DePristo, 1990; Ungerleider & Mishkin, 1982; Van Essen & Maunsell, 1983). In the dorsal stream, information passes through area MT to posterior parietal cortex (area PG, which is included in Brodmann's area 7). This pathway supports perception of spatial relations and motion and visuospatial attention (Andersen, Essick, & Siegel, 1985; Butters & Barton, 1970; Goldberg & Bruce, 1985; Lynch, Mountcastle, Talbot, & Yin, 1977; Mountcastle, Lynch, Georgopoulos, Sakata, & Acura, 1975; Robinson, Goldberg, & Stanton, 1978; Warrington & James, 1967). In the ventral stream, information flows through area V4 via TEO (Brodmann's area 37) to inferior temporal cortex (area TE, which corresponds approximately to Brodmann's areas 20 and 21). This pathway supports object recognition and color perception (Desimone, Albright, Gross, & Bruce, 1984; Gross, Kochar-Miranda, & Bender, 1972; Lansdell, 1968; Milner, 1958).

Recently, Arnold et al. (1991) and Bouras et al. (1994) examined the topographic and neuroanatomic distribution of neurofibrillary tangles (NFT) and neuritic plaques (NP) in cortical areas of AD brains. NFTs were far more dense in the temporal than in the parietal lobe. In particular, areas 20, 21, and 37 (temporal lobe) had higher NFT densities than areas 7, 39, and 40 (parietal lobe). Although there was considerable variance in the group data, the relative relation was preserved within individual participants. This pattern of cortical neuropathology suggests that visual capacities mediated by the ventral system will be more impaired than those mediated by the dorsal system. To date, no study has compared directly the relative functional integrity of these high-order visual areas in AD.

Method

Participants

Eleven participants with probable AD and 16 elderly controls participated in the study (see Table 1). The selection of AD patients was based on the antemortem clinical diagnostic guidelines of the National Institute on Aging (Khachaturian, 1985) and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984). All AD patients received a neurological examination, either magnetic resonance or computed tomography brain scan, and laboratory tests to rule out other causes of dementia.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of Alzheimer's Disease (AD)</th>
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<tr>
<td>Patients and Controls</td>
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<tr>
<td>Group</td>
<td>Age</td>
</tr>
<tr>
<td>Control</td>
<td>16</td>
</tr>
<tr>
<td>AD</td>
<td>11</td>
</tr>
</tbody>
</table>

Note. BDS = Blessed Dementia Scale.

The severity of dementia in the AD patients, assessed with the information, memory, and orientation section of the Blessed Dementia Scale (BDS; Blessed, Tomlinson, & Roth, 1968), ranged from scores of 0 to 21 (M = 11.9; maximum possible score = 37).

AD patients' spouses and other community volunteers comprised the control group. BDS scores for the control group ranged from 0 to 2 (M = 0.7). The AD and control groups did not differ significantly in age (p = 0.37; range = 58-83) or years of education (p = 49; range = 12-20). The best-corrected 14 in. (35.5 cm) visual acuity (Snellen) for all participants ranged from 20/20 to 20/30. The visual acuities of the AD patients did not differ from those of the controls.

Neuro-Ophthalmologic Examination

All participants in the study underwent a neuro-ophthalmologic examination, which included measures of Snellen acuity and refractive error, Goldmann perimetry, pupillary function, extraocular motility, slit-lamp examination to primarily detect cataracts, measures of intra-ocular pressure, and funduscopy to primarily assess the appearance of the macula and optic nerve. An assessment of gross visuospatial-motor coordination was made by observation and by judging the accuracy of touching or grasping objects in response to commands.

Procedure

The AD patients and controls received eight tests that probed capacities associated with either the ventral or dorsal processing streams. All tests have been shown previously to be selectively associated with a particular stream. In order to assess visual capacities relatively uncontaminated by general effects of dementia, we chose tests that minimize demands on memory, language, and other high-order cognitive processes. Each participant received the complete series of tests over a period of 2 to 3 days. Each test began with a demonstration followed by practice trials.

Visual Capacities Mediated by the Dorsal Processing Stream

Participants received four tests of visuospatial abilities: Mental Rotation, Money Standardized Road-Map Test, Stick Test, and Discrimination of Spatial Position. The background and procedure are described separately for each test.

Mental rotation. Posterior parietal cortex supports the ability to rotate objects mentally in space (Butters, Barton, & Brody, 1970; Butters, Soeldner, & Fedio, 1972; Butters & Barton, 1970). Specifically, patients with parietal-lobe lesions made significantly more errors selecting from four alternatives a geometric figure that matched a standard that was rotated 180° (Butters et al., 1970; Butters & Barton, 1970). A similar mental rotation test based on a test from the Luria-Nebraska Neuropsychological Battery (Golden, Hamecke, & Purisch, 1980) was used in the present study.

Stimuli were presented on a computer monitor. Participants viewed a test square that contained a darkened edge and a dot that was offset
to one side of the square. Adjacent to the test square were four similar squares. Participants indicated which of the four adjacent squares, when rotated, was identical to the test square with respect to the location of the dot and darkened edge. Test scores indicated the number correct out of 10 trials.

**Money Road-Map Test.** Spatial direction abilities were assessed by a test of direction sense (Money, 1976). It has been reported that patients with right parietal-lobe lesions made more than twice as many errors on the Money Road-Map Test than did patients with left or right temporal-lobe lesions (Butters et al., 1972). In this test, participants viewed an array of triangles, squares, and rectangles that were separated by spaces. A line extended along a path that coursed around the geometric shapes. While holding the map at a constant orientation, participants indicated verbally whether the angle of the path turned to the right or to the left. Scores were the number correct out of 32 direction changes indicated in the map.

**Stick Test.** In previous studies, patients with parietal-lobe lesions made significantly more errors on a test requiring the reconstruction of stick patterns that were rotated 180° from a standard (Butters, Barton, & Brody, 1970; Butters, Soeldner, & Fedio, 1972; Butters & Barton, 1970). Temporal lobe lesions did not degrade performance on this task (Butters et al., 1972). The present study used a similar test. The test materials consisted of eight wooden sticks, each about 5 in. (12.7 cm) long, marked with black paint at one end. The participant and the examiner each had eight sticks. In the first part of the test, the examiner, sitting next to the participant, arranged his sticks into a standardized pattern. The participant was required to replicate the examiner's stick pattern, including the orientation of the black marks. In the second part of the test, the examiner sat across from the participant. The participant was then required to replicate the examiner's stick pattern from the perspective of the examiner, thereby requiring the participant to rotate the pattern 180° mentally. Each section of the test contained 5 trials. Test scores indicated the number correct out of 10 trials.

**Discrimination of spatial position.** Haxby et al. (1991) found that regional cerebral blood flow (rCBF) increased in lateral superior parietal cortex while participants indicated which of two patterns contained a dot in the same relative location as a sample pattern. The present study used an adaptation of the test. On a computer monitor, participants viewed four patterns of equal proportion that were arranged horizontally. Each square contained a black dot. The two dots were in either the same relative locations or differed in position by 1, 3, 5, 7, or 9 mm. Participants indicated whether the dots were in the same or different relative locations within the two squares. Scores were based on the number correct out of 24 trials.

**Visual Capacities Mediated by the Ventral Processing Stream**

Participants received four tests of object recognition: Mooney Closure Faces Test, Benton Facial Recognition, Wechsler Adult Intelligence Scale—Revised (WAIS-R) Picture Arrangement, and Discrimination of Complex Figures.

**Benton Facial Recognition.** Haxby et al. (1991) found that rCBF increased in the occipitotemporal area while participants indicated which of two photographed faces match a standard. A similar test of facial recognition (Benton, 1974) was used in the present study. Participants viewed cards on which several photographs of faces were depicted. Participants matched the face at the top of the card (standard) to one or more of six faces depicted below. Three sets of cards were used: the matched faces were front views, side views, and front views under different lighting conditions. Scores were based on the number of correct matches out of 54 possibilities.

**Mooney Closure Faces Test.** The Mooney Closure Faces Test assesses perceptual closure by requiring participants to identify high contrast pictures of faces in which redundancy of the pictures was reduced by eliminating contour lines. In previous studies, right posterior temporal lobe lesions impaired performance on this test (Lansdell, 1968; Newcombe, Ratcliff, & Damasio, 1987; Newcombe & Russell, 1969), whereas right posterior parietal lobe lesions did not (Newcombe & Russell, 1969). Participants viewed 51 transformed drawings of human faces and categorized each as depicting one of the following: a boy, a girl, a man, a woman, an elderly man, or an elderly woman. The score was the number of correct responses out of 51.

**WAIS-R Picture Arrangement.** Utility of object recognition was tested with a subtest of WAIS-R (Wechsler, 1981). It has been found that patients with temporal lobe lesions were impaired on the Wechsler Picture Arrangement tests compared with controls (Milner, 1954). In this test, participants viewed cards that contained simple line drawings. The cards in each trial when arranged in the correct sequence depict a logical succession of events. Participants received 10 trials that contained either three (one trial), five (six trials), or six (three trials) cards. Scores were based on the number correct out of 10 trials.

**Discrimination of complex figures.** Meier and French (1965) found that right temporal lobectomy impaired performance on a visual discrimination task reliant on identifying small differences in the contours of complex patterns. The stimuli and procedure used by Meier and French were adapted for the present study. On a computer monitor, participants viewed four patterns of concentric circles with fragmented outlines. Three of the patterns were identical, and one differed in the position of the fragmented components. Participants indicated which pattern differed from the other three. Scores were based on the number correct out of 24 trials.

**Results**

**Neuro-Ophthalmologic Examination**

Among the participants initially scheduled to participate in the study, 8 AD participants and 5 controls were precluded from testing because of primary ophthalmologic abnormalities unrelated to AD, leaving 11 AD participants and 16 controls from whom data were collected. Abnormalities discovered during the examination included incipient glaucoma and significant cataracts. No gross disturbance of visuospatial–motor ability was observed.

**Visual Capacities**

Scores were transformed to percentage correct on each of the tests (see Table 2). Test scores of AD patients varied widely, ranging from values similar to those of controls to values beyond three standard deviations below the ECS mean (see Figure 1). Univariate analysis (t test), adjusting for multiple test chance effects, indicated that the test scores of AD patients were significantly below those of controls on all tests, except the Money Road-Map Test and Discrimination of Spatial Position. On all eight tests, the scores of AD patients did not correlate significantly with BDS, suggesting that visual symptoms were not associated with the level of dementia but instead reflected specific visual capacities of individual patients.

A separate discriminant analysis was performed for each functional category of tests (ventral and dorsal stream function). In each case, a discriminant function was computed to derive the linear combination of the four test scores in each category that provided the greatest discrimination between the two participant groups. This function represented the weighted
Table 2
Mean Percentage Correct Scores for Each Visual Test for Alzheimer's Disease (AD) Patients and Controls

<table>
<thead>
<tr>
<th>Stream function</th>
<th>Ventral</th>
<th>Dorsal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closer faces</td>
<td>63.7</td>
<td>27.5</td>
</tr>
<tr>
<td>Facial recognition</td>
<td>15.4</td>
<td>10.4</td>
</tr>
<tr>
<td>Picture arrangement</td>
<td>83.3</td>
<td>70.7</td>
</tr>
<tr>
<td>Complex figures</td>
<td>4.3</td>
<td>10.9</td>
</tr>
<tr>
<td>Mental rotation</td>
<td>14.0</td>
<td>12.7</td>
</tr>
<tr>
<td>Map test</td>
<td>93.7</td>
<td>48.2</td>
</tr>
<tr>
<td>Stick test</td>
<td>6.5</td>
<td>37.6</td>
</tr>
<tr>
<td>Spatial position</td>
<td>19.2</td>
<td>53.6</td>
</tr>
</tbody>
</table>

Combination of the four variables that maximized the between-group variability relative to within-group variability. The analysis produced a single score for each participant for each functional category. We computed scores to have zero mean (across groups) and pooled within-group variances equal to one (see Figure 2). Overall, tests of object recognition were better at discriminating AD patients from controls than were tests of visuospatial abilities, although AD patients were significantly impaired on both sets of tests. For the four tests of ventral stream function, the standardized discriminant function was highly significant \((p < .0001)\); group membership (AD vs. control) accounted for 86% of the variance of the discriminant function. The relative importance for each test in discriminating the groups ranked from the Picture Arrangement Test (standardized discriminant coefficient of 0.73), to the Closure Faces Tests (coefficient = 0.57), to the Facial Recognition Test (coefficient = 0.25), and to the Complex Figures Test (coefficient = 0.10). For the four tests of dorsal stream function, the standardized discriminant function was also significant \((p < .004)\), and group membership accounted for 48% of the variance. The Stick Test was by far the most robust among the visuospatial tests in discriminating group membership (coefficient = 1.09), followed by the Road-Map Test (coefficient = 0.17), the Spatial Position Test (coefficient = −0.15), and the Mental Rotation Test (coefficient = −0.17).

Discussion

These results demonstrate impairment in AD of visuospatial abilities and object recognition. The relatively greater deficit in object recognition supports the hypothesis that the cortical ventral stream, specialized for object recognition, is more
affected in AD than the dorsal stream, which is specialized for visuospatial abilities. All participants had normal acuity and no signs of ophthalmologic disease, thereby precluding the possibility that peripheral sensory dysfunction significantly contributed to perceptual impairment. Furthermore, participant groups were demographically matched and did not differ significantly in age. Ophthalmologic abnormalities associated with aging should therefore have occurred with equal likelihood in the two groups, and differences in performance could be attributed to participant group. Furthermore, dysfunction appeared to reflect specific perceptual impairment and not global aspects of dementia. In this regard, all AD patients were mildly to moderately affected and lived at home. The vision tests were selected to minimize the influence of general cognitive decline associated with dementia, including memory, and were not specific to visual perception.

The eight visual tests used delineated two basic categories of cortical visual function: object recognition and visuospatial abilities. Previous research with the eight tests established their specificity in measuring functions of either the ventral or dorsal visual streams. The administration of a complete set of tests from both functional categories to each participant allowed a comparative analysis of dorsal and ventral visual streams. All but two tests of visuospatial ability and all tests of object recognition distinguished the two participant groups, revealing a marked impairment of higher visual function in patients with AD. Furthermore, the analysis of the two categories of visual function indicated a relatively greater impairment of object recognition abilities. These results are consistent with those from histological studies in which a greater relative degeneration of inferotemporal cortex than of posterior parietal cortex was found in AD (Arnold et al., 1991; Bouras et al., 1994).

The relatively greater vulnerability of visual function associated with the ventral processing stream is consistent with other reports. Mendola et al. (1995) investigated performance on tests measuring a diverse group of visual abilities in AD and found the highest prevalence of impairment on a test of backward pattern masking, followed by tests of spatial abilities and motion analysis. The greater vulnerability of pattern vision over spatial or motion perception was interpreted as reflecting relatively greater degeneration of inferotemporal cortex than of posterior parietal areas. Cronin-Golomb et al. (1995) also found a differentiation between object recognition and spatial localization abilities in AD. Based on the association between several vision tests and cognitive function, they found that cognitive tests for which visual performance was the best predictor of dementia were those that assessed object recognition. Furthermore, pattern masking was the best predictor of cognitive performance, followed by low spatial frequency contrast sensitivity, and color discrimination (specific to blue hues). These results suggest that AD has a differential effect on the two cortical processing streams.

In a prior study, we found that impaired visual function in AD did not reflect functions presumed to be preferentially mediated by either the magnocellular or parvocellular precortical channel (Kurylo et al., 1994) alone. Rather, impaired visual function in AD is more likely a consequence of lesions in extrastriate visual cortex. Primary connections through visual cortex link parvocellular layers of the lateral geniculate nucleus (LGN) to inferotemporal areas, whereas LGN magnocellular layers are linked to parietal areas (DeYoe & Van Essen, 1988). However, many cross connections exist between parvocellular and magnocellular processing streams in striate and extrastriate cortex, and recent evidence indicates that the parvocellular as well as magnocellular pathways provide input to areas MT (Maunsell et al., 1990) and V4 (Ferrera, Nealey, & Maunsell, 1994). It is clear that physiologically distinct precortical channels do not maintain functional segregation in high-order cortical areas (Nealey & Maunsell, 1994).

AD patients demonstrated deficits on both categories of tests, and performance across tests varied among individual participants. Impairment on object and spatial abilities reflects the cumulative effects of neuropathological changes in temporal lobe as well as parietal lobe areas. Although test categorization was based on theoretical considerations as well as previous research, high-order visual functions are not uniquely associated with specific cortical regions (Schiller, 1993). For example, cross-correlations among cortical areas, as revealed by measures of regional cerebral blood flow, have been found during performance of object vision and spatial vision tasks (McIntosh et al., 1994). Nevertheless, recent studies have demonstrated a functional dissociation of cortical processing streams for object recognition and spatial location in humans. Measurements of cortical function have demonstrated task-related increases in activation within extrastriate areas. Specifically, increases in regional cerebral blood flow as measured by PET occurred in occipitotemporal and lateral superior parietal cortices while participants performed face-matching or location-matching tasks, respectively (Haxby et al., 1991, 1994; Unger-
subject to parietal lobe function does not support the notion of parietal lobe hypoperfusion as a hallmark of early AD. Although visual impairment may be the predominant symptom in early stages of AD, visual dysfunction varies in prevalence and severity across cases. Subgroups of patients have been identified in which impairment is specific to either semantic language function or visuospatial abilities (Martin et al., 1986). Cases of specific preponderant cognitive deficits in language and visuospatial abilities have been associated with diminished rates of glucose metabolism localized to left hemisphere and right parietal cortex, respectively (Foster et al., 1983). Furthermore, PET measurements have delineated AD into subgroups that are distinguished by their profile of metabolic rates across cerebral areas (Rapoport et al., 1991). Individual cases of visuospatial deficits found here may reflect parietal lobe dysfunction specific to those participants.

Widespread neuropathological changes exist across cortical association areas in AD, although the relative density of neuropathological changes varies among regions (Arnold et al., 1991). The pattern of degeneration and the associated functional impairments that result may reflect the progression by which neuropathological changes invade cortical areas. There is a hierarchical pattern of lesion distribution in AD that is specific to neurofibrillary tangles (NFT) and the deposition of senile plaques. There is also a characteristic pattern of spread over time in which NFT initially affect hippocampus and entorhinal cortex and then progress to invade inferotemporal and parietal areas at later stages of the disease (Arriagada, Growdon, Hedley-Whyte, & Hyman, 1992). Abnormalities on tests that assess the functional integrity of specific brain regions offer a window into the spread of AD lesions. When the cortical lesions are focal, AD patients manifest prominent visual symptoms (Cogan, 1985; Kiyosawa et al., 1989; Levine et al., 1993; Sadun et al., 1987), at times characterized by specific impairment in either object recognition (Cogan, 1985) or visuospatial abilities (Cogan, 1979). Cases have been reported in which visual dysfunction specific to either the ventral or dorsal processing streams reflected specific neuropathological changes in each of these cortical regions (Hof & Bouras, 1991; Hof et al., 1989, 1990). The pattern of perceptual impairment measured on tests given here may also reflect the regional distribution of neuropathological changes in visual cortical areas in each individual. Alternatively, variability may reflect distinct courses of cortical degeneration or may reflect different forms of the disease (such as Apo E genotype; Liddell, Williams, Boyer, Kaiser, & Owen, 1994; or the presence of major gene AD; Van Duijn, Farrer, Cupples, & Hofman, 1993). We found that test performance did not correlate with the severity of dementia as measured by the Blessed Dementia Scale. This finding suggests that visual dysfunction does not follow overall disease progression but instead reflects the heterogeneous nature of the neuropathological changes.

References


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