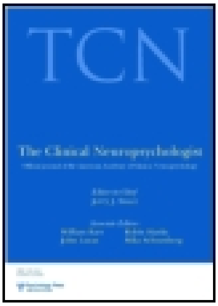

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Error Analysis of the Nine-Word California Verbal Learning Test (CVLT-9) Among Older Adults With and Without Dementia

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ABSTRACT

The nine-word California Verbal Learning Test (CVLT-9; Libon et al., 1996; Spreen & Strauss, 1998) is a verbal list learning task used to assess declarative memory impairment among dementia patients. The present study sought to investigate the neuro-cognitive mechanisms that underlie the production of intrusions and perseverations on the list A, free recall learning trials, and the false positive responses made on the delayed recognition condition. Patients with probable Alzheimer's disease (AD), Ischaemic Vascular Dementia associated with periventricular and deep white matter changes (IVD), and individuals without dementia (NC) were studied. Between-group analyses showed that AD participants produced more initial intrusion errors, and perseverated on those same intrusion errors across list A learning trials than IVD or NC participants. Also, as participants with dementia produced initial free recall intrusion errors, the semantic organization of their responses on the 'animal' word list generation task declined (Giovannetti-Carew, Lamar, Cloud, Grossman, & Libon, 1997). On the delayed recognition test condition, within-group analyses revealed that the IVD group endorsed more list B interference foils, than other errors. AD participants endorsed semantically related foils and list B interference foils. In addition, as participants with dementia endorsed more list B interference foils, more perseverations were produced on the Graphical Sequence Test – Dementia Version (Lamar et al., 1997). These results were interpreted within the context of the semantic knowledge, and executive functions deficits that typify AD and IVD, respectively.

INTRODUCTION

Alterations in memory are associated with all dementia syndromes. For example, an anterograde amnesia at the encoding level typifies the memory disorder seen in Alzheimer's disease (AD). Thus, on serial list learning tasks, such as the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987) patients with AD often evidence little learning on immediate free recall test trials, produce copious intrusion errors on free and cued recall test trials, demonstrate little savings after a delay, and do not benefit from cuing when assessed with a delayed recognition test. This pattern of memory impairment has been associated with a proliferation of neurofibrillary tangles and senile plaques in the medial temporal lobe (Delis et al., 1991; Libon et al., 1998).

Alterations in memory and learning, as assessed with serial list learning tasks, have also been observed in other dementing illnesses such as Parkinson's disease (PD) and Huntington's disease (HD). When these so-called 'subcortical' dementing syndromes have been compared to

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AD, patients with moderate to severe HD recalled more words from the list A, immediate free recall test trials, but produced fewer intrusion errors (Kramer et al., 1988). Delis and colleagues (1991) found that patients with AD and HD were comparable with respect to their total recall on the list A, immediate free recall test trials. Nonetheless, patients with HD made fewer intrusion errors on cued recall test trials, and obtained higher delayed free recall and recognition discriminability scores than patients with AD. Similar profiles have sometimes been observed among some patients with PD (Filoteo et al., 1997; Massman, Delis, Butters, Levin, & Salmon, 1990).

Past research has suggested that the profile of impairment in memory and learning among patients with Ischaemic Vascular Dementia (IVD) associated with periventricular and deep white matter alterations is very similar to the pattern of deficits produced by patients with HD and PD. For example, as compared to patients with AD, patients with IVD exhibit a comparable level of impairment on immediate free recall test trials. Like patients with HD and PD, however, patients with IVD produced fewer intrusion errors, and higher delayed free recall savings and recognition discriminability scores (Libon et al., 1997, 2001). Moreover, similar to patients with HD and PD, patients with IVD have been shown to display greater impairment on tests of procedural learning as compared to patients with AD (Libon et al., 1998).

The constructs that underlie this pattern of impairment on verbal serial list learning tasks are not clearly understood. For example, patients with AD are known to suffer from a degradation of lexical access and/or loss of semantic knowledge (Chan et al., 1995; Giovannetti-Carew et al., 1997; Schwartz, Marin, & Saffran, 1979). However, the degree to which lexical access or semantic knowledge impairment may contribute to deficits in declarative memory is unclear. Alternatively, past research has shown that executive control dysfunction is associated with impairment on paradigms designed to assess memory and learning (Freedman & Oscar-Berman, 1986). Duke and Kasniak (2000) have pointed out that executive control deficits are present in virtually all patients with degenerative dementing illnesses. Indeed, Vanderploeg, Schinka, and Retzlaff (1994) have demonstrated a modest, but statistically significant relationship between free and cued recall test performance on the CVLT, and performance on tests of executive control (Trail Making Test – Part B) and attention (Digit Span). In sum, it appears that, among other factors, both semantic knowledge and executive functioning share a portion of the variance for verbal list learning performance.

Hypotheses and Predictions

In the present study patients with AD and IVD, and a normal control group (NC) were studied. The purpose of this investigation was twofold. First, from the standpoint of clinical utility, we sought to provide a finer grain analysis of intrusion errors and perseverations produced on the CVLT-9 immediate free recall learning trials, and of the pattern of false positive responses made on the delayed recognition test condition. Second, we wished to investigate the underlying neurocognitive mechanisms that may be associated with the production of these errors by examining errors made by patients with IVD, AD and non-demented elders.

Can an intrusion also be a perseveration? We believe that the traditional operational definition of immediate free recall intrusions and perseverative errors may obscure some manifestations of executive control dysfunction on serial list learning tasks. For example, it has been shown that patients with AD tend to produce many extra-list intrusion errors on the CVLT (Libon et al., 1996). In the present research we use the term *initial intrusion* to describe the first time an intrusion error is made. However, using the traditional scoring method of Delis and colleagues (1987) so-called *initial intrusions* that are repeated on subsequent learning trials are scored as intrusion errors, *despite the notion that they reflect perseverative behavior.* In the present research, we use the term *trans-trial perseveration* to describe intrusion errors on the immediate free recall learning trails that re-occur on later immediate free recall learning trials. Deficits in semantic knowledge have been associated with the production of intrusion errors made on declarative memory tasks (Lafosse et al., 1997).

When Butters, Granholm, Salmon, and Grant (1987) asked patients with AD and HD to recall prose passages, only patients with AD produced a significant number of intrusion errors from previously presented stories. Similarly, patients with AD produced more perseverations on tests of verbal fluency than patients with HD. They interpreted these findings as associated with deficits in semantic knowledge. On the basis of these findings, our first prediction was that patients with AD will produce more *initial intrusions*, as well as *trans-trial perseverations* than patients with IVD, and these errors will be highly correlated with measures of semantic knowledge.

A third type of error made by dementia patients on CVLT immediate free recall learning trials is to repeat a response, either correct or incorrect, that was produced earlier in the learning trial. We use the term *within trial perseveration* to describe this behavior. Stuss and colleagues (1994) found that patients with right frontal lobe lesions made significant numbers of this type of error on experimental verbal serial list learning tasks. Moreover, previous research has consistently shown that patients with IVD associated with periventricular and deep white matter alterations are particularly disadvantaged on tests of executive function (Libon et al., 1997, 2001). On the basis of this research we speculate that impaired executive processes may underlie the lapses in self-monitoring, thus leading to the production of these errors. Thus, our second prediction is that patients with IVD will produce more *within trial perseverations*, and that *within trial perseverations* will be highly correlated on measures of executive function.

Different patterns of performance on the CVLT delayed recognition condition have been reported among patients with dementia (Filoteo et al., 1997; Woodard, Goldstein, Roberts, & McGuire, 1999), schizophrenia (Kareken, Moberg, & Gur, 1996), and alcoholism/poly-substance abuse (Bondi, Drake, & Grant, 1998). Moreover, Libon and colleagues (1996) reported that patients with IVD obtain a higher recognition discriminability index than AD patients on the CVLT-9. However, this study did not describe the types of recognition foils endorsed by each group. Thus, in the present research we sought to systematically examine the distribution of false positive errors on the CVLT recognition test condition. Because the executive functioning deficits seen among patients with IVD may lead to difficulty in organizing newly encoded information, our third prediction was that IVD participants will endorse more foils from the list B, interference trial, and that list B recognition foils will be correlated with tests of executive control. By contrast, semantic knowledge deficits are highly associated with AD. With the progressive degradation of semantic knowledge AD patients might have difficulty in distinguishing the attributes of exemplars from shared categories contained in both list A and list B word lists. Thus, we also predict that patients with AD will endorse more semantically related recognition foils, and that these false positive responses will be correlated with tests of semantic knowledge.

METHODS

Participants

One hundred and four participants (54 AD; 50 IVD) were drawn from the Alexander Silberman Center's Geriatric Assessment Program (GAP) at Crozer Chester Medical Center. GAP participants were excluded if their medical records and structured patient interviews indicated history of head injury, substance abuse (including alcohol), exposure to known neuro-toxins, major psychiatric disorders (including major depression, hallucinations, delusions), epilepsy, B12, folate, thyroid deficiency, or Parkinson's disease. GAP participants were assigned to clinical groups by meeting either the NINCDS-ADRDA criteria for probable AD (McKhann et al., 1984), or the CADDTC criteria for possible and probable IVD (Chui et al., 1992). Of the 104 participants with dementia, 7 patients with AD and 11 patients with IVD could not complete all portions of the CVLT-9. These participants were excluded from the present study. Thus, the final sample consisted of 47 patients with AD and 39 patients with IVD. The duration of illness among patients ranged between 2.5 and 3.5 years, per interview with family members of patients. Also, there was no difference between dementia groups in the distribution of their Clinical Dementia Rating Scale scores (Berg, 1988; AD – CDR .5 $n = 2$, CDR 1 $n = 41$, CDR 2 $n = 4$; IVD – CDR .5 $n = 2$, CDR 1 $n = 34$, CDR 2 $n = 2$).

Nondemented elders (NC, $n = 39$) were recruited from several retirement communities. They were included in the study if their scores on the Mini-Mental

Table 1. Demographic and Neuropsychological Measures (Means and Standard Deviations).

	AD	IVD	NC
Age	76.74 (5.83)	79.10 (6.29)	74.85 (7.16)
Education	12.28 (2.35)	11.08 (2.51)	14.56 (2.95)
MMSE	21.34 (3.58)	21.67 (4.26)	28.82 (1.14)
GDS	5.19 (4.29)	6.64 (4.46)	2.82 (3.00)
Percent female	58.2	55.8	85.6
'animal' WLG AI	2.73 (0.84)	3.35 (0.84)	
Graphical Sequence Test	8.18 (7.35)	15.85 (10.25)	

Note. AD = Alzheimer's disease; IVD = ischaemic vascular dementia; NC = normal control; MMSE = Mini-Mental State Examination; GDS = Geriatric Depression Scale; WLG AI = Word List Generation Association Index.

Status Exam (MMSE; Folstein, Folstein, & McHugh, 1975), and Geriatric Depression Scale (GDS; Yesavage, 1986) were >27, and <10, respectively.

No differences were noted between the two dementia groups in age, education, or in their performance on the MMSE or GDS scores (Table 1). When the dementia and NC groups were compared, participants with IVD were older than the NC group (Tukey, $p < .009$). In addition, both AD and IVD participants obtained higher scores on the GDS, and had fewer years of education than the NC group (GDS – Tukey, AD vs. NC, $p < .001$; IVD vs. NC, $p < .001$; education – AD vs. NC, $p < .001$, AD vs. IVD, $p < .001$). However, correlational analyses between these demographic variables and performance on the CVLT measures of interest were not statistically significant. Thus, we did not to co-vary these variables on subsequent analyses.

Materials, Procedure & Scoring

The CVLT-9 was administered according to standard procedures (Delis et al., 1987; Libon et al., 1996) by graduate students enrolled in doctoral level clinical psychology training programs who were blind to the hypotheses and predictions listed above. As noted above, participants who could not complete all portions of the CVLT were not included in any analyses. The following supplemental variables were coded.

Free Recall Errors

Initial Intrusions: This was defined as the number of unique (i.e., nontarget) words produced on free recall test trials. For example, if the word 'apple' were to appear on trials 3, 4, and 5, only the first occurrence of this error was scored as an initial intrusion on trial 3.

Trans-Trial Perseverations: This was scored when initial intrusions were repeated on subsequent learning trials. Although 'apple' might appear on trials 3, 4, and 5, only two trans-trial perseverations would be scored (trial 4 and 5).

Within Trial Perseverations: This was scored when initial intrusion errors were repeated within each individual learning trial. This type of error included perseverations of both nontarget words (e.g., 'apple') and correct target words on each free recall learning trial. This variable is equivalent to Delis and colleagues' (1987) definition of perseveration.

Recognition Errors

Semantic False Positive Foils: These nontarget extra-list foils were from the same three semantic categories as the original target words from list A, and constitute highly prototypic exemplars (Rosch, 1975; i.e., apples, oranges, pants, socks, carrots, & corn; $n = 6$).

Interference (List B) Foils: These foils were drawn from the list B, interference condition. These foils are comparable in lexicon frequency to the target items (Rosch, 1975; strawberries, peaches, brownies, cookies, drill, wrench; $n = 6$).

Unrelated False Positive Foils: These foils are neither semantically similar, nor included in the interference condition (glasses, soap, mop, racquet, keys, rug, radio, roses, drapes, pencil, wallet, baggage; $n = 12$).

Neuropsychological Assessment

The CVLT-9 was administered to dementia patients within the context of a comprehensive neuropsychological protocol. Semantic knowledge was assessed with the 'animal' word list generation test (WLG; Giovannetti-Carew et al., 1997). On the 'animal' WLG, participants were given 60 s to generate the names of animals. The dependent variable derived from the 'animal' WLG was the Total Association Index (AI). The AI measures the degree to which successive responses are semantically related. It is calculated by summing the shared attributes from successive responses and dividing that number by 1 minus the total number of responses generated, thus controlling for total output. A high AI is believed to reflect intact semantic memory stores. Complete details regarding how this measure was derived and scored can be found in the study by Giovannetti-Carew et al. (1997).

Executive control was assessed with the Goldberg Graphical Sequence Test – dementia version (GST–D; Lamar et al., 1997). On the GST–D patients were asked to draw geometric shapes and letters. At various times throughout the test patients must switch their mode of output, that is, instead of drawing shapes, patients are required to write sentences with the words 'circle,' 'square,' and so on. The dependent variable was the total number of perseverations. Complete details regarding how perseverations are identified and scored can be found in the study by Lamar et al. (1997). Only participants with dementia were administered these tests.

RESULTS

Free Recall Error Analysis

A multivariate analysis of variance was conducted with group (AD, IVD, NC) as the independent variable, and performance with respect to CVLT-9 free recall initial intrusion errors, trans-trial, and with-trial perseverations as the dependent variables. This analysis yielded a significant multivariate main effect for group ($F[6, 238] = 6.24$, $p < .001$), and significant follow-up univariate ANOVAs for initial intrusion, trans-trial, and within trial perseverations (initial intrusions – $F[2, 122] = 13.27$, $p < .001$; trans-trial perseverations – $F[2, 122] = 6.06$, $p < .003$; within trial perseverations – $F[2, 122] = 4.41$, $p < .014$). Partial evidence in support of our first prediction was obtained. Post hoc analyses (Tukey tests) revealed that the AD group made more initial intrusions and trans-trial perseverations than the IVD and NC groups (initial intrusions – AD vs. IVD, $p < .001$; AD vs. NC, $p < .001$; trans-trial perseverations – (AD vs. IVD, $p < .010$; AD vs. NC, $p < .007$). The IVD and NC group did not differ on either of these measures. Furthermore, virtually all intrusions were exemplars of the semantic categories for all dementia patients. There were no between-group differences on the incidence of prototypic initial intrusions (e.g., 'apple'; Rosch, 1975) between the dementia groups. However, if an initial intrusion was prototypic of a semantic category, it was always endorsed on recognition trial. Also, consistent with our first prediction, as dementia participants made more *initial intrusions* they obtained a lower 'animal' AI ($r = -.276$, $p < .008$). There were no statistically significant differences between groups for *within trial perseverations*.

Analysis of Long-Delay Recognition Trials

The multivariate effect for group (AD, IVD, NC) was highly significant ($F[6, 238.] = 24.78$, $p < .001$), and univariate ANOVAs yielded a significant effect for group for the semantic ($F[2, 122] = 47.27$, $p < .001$), list B ($F[2, 122] = 45.61$, $p < .001$), and unrelated foils ($F[2, 122] = 28.13$, $p < .001$). Post hoc between-group comparisons (Tukey tests) revealed that the AD group endorsed more semantic foils as compared to IVD ($p < .001$), and NC groups ($p < .001$); however, there was difference between the IVD and NC groups on this measure. For list B foils there was no difference between the AD and IVD groups, however, both dementia groups endorsed more list B foils as compared to the NC group (AD vs. NC, $p < .001$; IVD vs. NC, $p < .001$). Finally, for the unrelated foils the AD group endorsed more of these foils as compared to the IVD and NC groups (AD vs. IVD, $p < .001$; AD vs. NC, $p < .001$). There was no difference for unrelated foils when the IVD and NC groups were compared.

Consistent with our third prediction, within-group post hoc analyses (significance $p < .01$) indicated that IVD participants endorsed more list B foils as compared to semantic (paired $t[38] = 3.10, p < .004$) and unrelated foils (paired $t[38] = 5.24$, $p < .001$, Table 2). However, AD participants endorsed semantic and list B foils, with comparable frequency. Also, partial support for our third prediction was found in that as dementia participants endorsed more list B recognition foils, more GST–D perseverations were produced [$r = .358$, $p < .001$].

DISCUSSION

In previous research, Libon and colleagues (1996, 1997, 2001) demonstrated that individuals with AD and IVD produced the same number of

Table 2. Free Recall and Recognition Errors (Means and Standard Deviations).

	AD $n = 47$	IVD $n = 39$	NC $n = 39$	Significance
Free recall errors (trials 1–5)				
Initial intrusions	1.31 (1.77)	0.38 (0.63)	0.10 (0.30)	AD > IVD = NC
Trans-trial perseverations	0.78 (1.45)	0.15 (0.67)	0.12 (0.46)	AD > IVD = NC
Within trial perseverations	0.51 (0.77)	1.00 (1.52)	0.92 (1.19)	AD = IVD = NC
Percent of participants making free recall errors				
Initial intrusions	31 (66%)	16 (41%)	4 (10%)	
Trans-trial perseverations	16 (34%)	4 (10%)	3 (8%)	
Within trial perseverations	21 (45%)	23 (59%)	18 (54%)	
Recognition errors (between-group)				
Semantic foils	3.38 (1.42)	1.46 (1.64)	.62 (0.91)	AD > IVD = NC
List B foils	2.81 (1.47)	2.13 (1.66)	.15 (0.43)	AD = IVD > NC
Unrelated foils	2.49 (2.00)	.97 (1.46)	.13 (0.34)	AD > IVD = NC
Recognition errors (within-group)				
AD semantic foils = list B foils > unrelated foils				
IVD list B foils > semantic foils > unrelated foils				
NC list B foils = semantic foils = unrelated foils				

Note. AD = Alzheimer's disease; IVD = ischaemic vascular dementia; NC = nondemented control.

correct responses on CVLT-9 free recall (list A) learning trials. However, patients with AD made more intrusion errors on these learning trials as compared to other dementia patients, and endorsed more false positive responses on the delayed recognition task. The current investigation attempted to more clearly define these CVLT-9 errors according to hypothesized mechanisms that may underlie their production.

Free Recall Errors: 'Intrusions and Perseverations' Revisited

Consistent with previous research, between-group analyses revealed that individuals with AD made more *initial intrusions* during the free recall learning trials than those with IVD. However, not only did AD participants make more *initial intrusions* than the IVD between-group analyses indicated that patients with AD also repeated these same intrusions (*trans-trial perseverations*) throughout the free recall (list A) learning trials. By contrast, there was no between-group difference among dementia patients in their production of *within trial perseverations*. This finding implies that the traditional operational definition of intrusion errors (Delis et al., 1987) appears to include aspects of perseverative behavior. Thus, the present investigation demonstrates that individuals with AD exhibit a type of perseverative behavior on the CVLT-9 that has previously not been appreciated, albeit in a distinct manner from those with IVD.

Delis and colleagues (1987) have made the distinction between 'proximal' and 'distal' perseverations. Distal perseverations are more indicative of an amnestic syndrome, whereas proximal perseverations are often associated with frontal lobe pathology (Luria, 1980). In the present study, we found no between-group differences in the 'distance' between the first and second occurrence (i.e., *within trial perseveration*) of a target word. Nonetheless, the *trans-trial perseverations* produced by patients with AD might be considered distal from the original utterance of the intrusion (i.e., carried to the next trial), and therefore characteristic of the amnestic syndrome in AD.

Neuro-Cognitive Mechanisms: The Role of Semantic Knowledge and Executive Control Deficits

On the free recall (list A) learning trials, AD participants' semantic knowledge deficits could make it difficult for them to distinguish target items from exemplars belonging to the various semantic categories contained in the word list.

Between-group analyses indicated that AD participants made more *initial intrusions*, as well as *trans-trial perseverations*. Furthermore, the vast majority of these intrusions were exemplars of the semantic categories. These errors were correlated with the 'animal' WLG Total Association Index, a measure of semantic integrity. Moreover, we found that virtually all individuals who made prototypic *initial intrusions* on the free recall (list A) learning trials (e.g., 'apples') endorsed these very same words on the delayed recognition test. This raises the question – would participants who make *initial intrusions* endorse their self-generated responses on recognition testing if they were asked to discriminate their errors from target words? Unfortunately the design of the CVLT-9 does not provide for a systemic evaluation of this question.

IVD associated with periventricular and deep white matter alterations has been associated with hypoperfusion of the frontal lobes as measured with functional imaging techniques (Sultzer et al., 1995). In addition, we have demonstrated that patients with IVD are very disadvantaged on tests of executive function (Libon et al., 1997, 2001). We speculated that inconsistent self-monitoring may have been responsible for the production of *within trial perseverations*. However, no between-group difference was found on this measure.

Delayed Recognition Errors

The types of recognition false positive responses endorsed by patients with AD and IVD were different. In general, between-group analyses indicated that patients with AD made more false positive responses than IVD or NC participants. Nonetheless, the within-group analyses were significant for some dissociations. Consistent with our third prediction, patients with IVD endorsed more list B foils than semantic or unrelated foils. By contrast, patients with AD endorsed both semantic and list B foils more frequently than unrelated foils. This likely represents the combination of a primary amnesia (i.e., rapid forgetting), as well as the possible impact of compromised semantic networks. Furthermore, this finding indicates that the lower recognition discriminability index typical of AD is due to endorsement of both semantic and list B foils. Moreover, consistent with our third prediction, correlational analyses revealed that as dementia participants endorsed more interference (list B) recognition foils, they produced more total perseverations on the GST–D.

When these data are assessed as a whole, we believe that deficits in semantic knowledge and executive control are responsible for the pattern of intrusions, perseverations, and false positive responses on CVLT-9 free recall (list A) learning and recognition test trials. Indeed, as Luria (1980) postulated, perseverations occur in domains of cognition in which patients are experiencing their deficits. Thus, the errors produced on the CVLT-9 by patients with AD appear to be related to their semantic knowledge deficits, while the errors produced by patients with IVD may be associated with deficits in executive dysfunction.

Long-Delay Recognition Testing: Support for an Interference Trial

These results underscore the utility of employing a declarative list learning procedure with an interference condition. By presenting the list B, interference learning trial, we determined that participants with IVD were drawn to this list when asked to distinguish target from nontarget words. The tendency to endorse items from the interference (list B) condition accounts for the diminished recognition discriminability index of IVD persons with when compared to nondemented elders. Without an interference paradigm (e.g., Hopkins Verbal Learning Tests; WMS III; CVLT-2 Mental Status Form), such deficits would go unnoticed.

Limitations and Future Research

This investigation is not without its limitations. The conclusions drawn from the comparisons between the IVD, AD and NC groups are somewhat attenuated by the fact that women were disproportionately represented in the NC cohort. Also, a restriction in range may be present with respect to the production of free recall intrusion errors and perseverations, and recognition false positive responses. This suggests that clinical decisions made on the basis of these data should be made with caution. Finally, although our data suggest that impairment in semantic knowledge and executive control appear to underlie the differential pattern of errors on the CVLT-9, the test was not originally designed to elucidate these constructs. Thus, the development of tests and procedures that further assess semantic knowledge and executive skills is necessary to validate our findings. Such research is currently underway in our laboratory.

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