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# Differential characteristics of the aging process and the vascular cognitive impairment in the organization of memory retrieval

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ABSTRACT

Early identification of cognitive impairment in patients with chronic cerebral vascular disorders can allow for evaluating the time course of the disease up to the phase of conversion to dementia. The specific indicators of pathological cognitive decline should be identifiable vs. the concurrent age-associated changes in memory which accompany the aging process.
We propose a method which evaluates memory dysfunctions in vascular cognitive impairment (VCI) as distinct from age-associated memory changes. This method is based on a serial learning task of concrete frequent words and it consists in controlling the effects of age and cerebral pathology on various characteristics of immediate recall, including serial effect and productivity.
Ninety participants underwent a between group examination: younger adults vs. older adults vs. VCI patients who were outpatients with a positive history for chronic cerebral vascular disorder, positive neuroimaging examination, a Hachinski ischemic score ≥ 5 and a mild to moderate cognitive impairment.
VCI patients show a reduced efficiency of retrieval and recall organization while, age-associated cognitive changes consist of a modification of the serial position effects. In particular, VCI patients, as distinct from same-age normal cases, can perform an only partial utilization of the inherent structure of the memory task with a very limited efficiency of relearning which is not sufficiently supported by the facilitating factors due to task repetition.



## 1. Introduction

The term vascular cognitive impairment (VCI) describes significant cognitive difficulties that arise from vascular causes [1]. VCI includes clinical subtypes which are heterogeneous according to the level of cognitive and behavioral impairment, clinical course, underlying pathogenic mechanisms and processes, and neuro-anatomical correlates. The main classification defines three principal groups: vascular dementia, AD with a vascular component (mixed dementia), and vascular cognitive impairment with no dementia (VCI-ND) [2]. Specifically, the diagnosis of VCI-ND classifies patients with cognitive impairment who do not meet the criteria for dementia but have increased risks for converting to dementia and for institutionalization and death [3,4]. The early identification of cognitive impairment in patients with cerebral vascular disorders is of particular clinical utility for activating prompt therapeutic interventions to correct concurrent conditions underlying the progression of the disease and for minimizing the risk for conversion to vascular dementia. The presence of memory disorders in VCI patients for several years can lead to the diagnosis of dementia [5–9].

Brain volumetric studies often present inconclusive evidence of a specific relationship between brain size (i.e. cortex and/or other sub-cortical structures) and memory functioning [10]. Those studies which have tried to separate the age-dependent effects from dementia-specific conditions have shown that age-related volumetric effects of the brain consist in a reduction of the temporal and frontal lobes' gray matter and that these findings are correlated to memory performance. White matter hyperintensities which are considered pathological signs [11] are also correlated to a decreased memory functioning. According to these findings, brain atrophy and subcortical vascular disease might be considered independent factors affecting memory functioning [12].

Episodic memory measures derived from free recall tasks and in particular, measures derived from cue-recall and free recall paradigms, significantly contribute to predict conversion to dementia [5]. Measures obtained by the free recall paradigm are in general measures of productivity, the traditional measures concerning the final output of the memory process activated by the free recall tasks. They allow for limited inferences on the underlying encoding, inhibition, search and retrieval processes which are critically implicated in the accuracy of retrieval.

To obtain more specific and articulated information on memory functioning, the measurement of free recall can be accompanied by quantitative indicators of recall organization, such as measures of serial position effects, which allow for in-depth relevant inferences on

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the encoding and retrieval processes. By analyzing the order in which subjects recall list items, the serial position analysis evaluates specific aspects of retrieval organization, such as the extent to which the sequential order of item recall (retrieval, or output position) differs from the order of presentation of the "to be recalled" list items (encoding or input position). Among the serial position effects experimentally identified so far, "primacy" refers to the increased probability to recall start-of-list items, and "recency" is the increased probability to recall end-of-list items [13]. Efficiency and organization in free recall primarily depend on the characteristics of the memory tasks, including instructions given to the subjects, and on cognitive strategies deliberately or unintentionally set in place by the subject to cope with the testing procedure. Memory task repetition, including repeated session of acquisition and recall of the study list, and the use of a structured word list have been shown to mediate free recall efficiency and organization [14–16].

There is a technical difficulty in differentiating age-related changes in cognitive functioning from those associated to pathological disorders of the aging brain. To date, there is no definitive consensus on where boundaries between disease and non-disease memory changes lie, or even if such a definite boundary genuinely exists [17]. Our study is aimed to evaluate a method for the assessment of memory dysfunction in vascular cognitive impairment (VCI) as different from the age-associated memory changes and to collect preliminary data on the clinical validity of this method. This is based on the standardized administration of sequentially-ordered, verbal–auditory, repeated tasks of immediate and delayed free-recall of a word list with an implicit semantic structure which should help in discriminating between quantitative changes in memory output from qualitative modifications associated to changes in memory processes' hierarchy.

## 2. Material and methods

### 2.1. Participants

Ninety Italian subjects, both sexes (M:F = 41:49), mean age 49.4 years (SD, 15.4), with average education level, gave consent to participate to the study, and were classified into three experimental groups: younger adults (N = 30, age range 20–39, M 28.8, SD 4.2), older healthy adults (N = 30, age range 50–69, M 59.2, SD 5.8), and vascular cognitive impairment (VCI) older adults (N = 30, age range 50–69, M 60.2, SD 4.9). VCI outpatients had a positive history for chronic cerebral vascular disorder (CCVD) with positive results at neuroimaging examination, supported by a Hachinski ischemic score ≥ 5 [18] (HIS; M 9.1, SD 3.2), no recent acute cerebral vascular episodes, a mild to moderate cognitive and behavioral impairment (Mini Mental State Examination total score, M 23.8, SD 3.4; Global Deterioration Scale: stage 3 = 80% of VCI patients, stage = 4, 20% of VCI patients), and with no diagnosis of dementia.

Each case underwent the administration of an experimental procedure consisting of the acquisition and immediate recall of a word list consisting of 16 high imagery and high frequency Italian words, clustered according to 4 different, mutually exclusive taxonomic categories, pseudo-randomly assigned to a serial position with the limitation that items belonging to the same semantic category would not be presented in contiguity. Word list was slowly read to the subject at a presentation rate of approximately 1 word per second.

Subjects were asked to recall as many words as they could in any order they wished. The sequence of memory tasks was administered as the following:

Task 1: acquisition and immediate recall of the word list, followed by a 3-minute interval with standardized distracters (participants were asked to perform a not-related to the word list picture recognition task);

Task 2: 2nd acquisition and immediate recall.

For each memory task, correct recalls and intrusions (false recall of items not belonging to the word list), and the order of recall of correct items were recorded.

### 2.2. Measures and statistical analysis

Efficiency of retrieval is measured as a differential score (correct recalls minus intrusions). An analysis of variance (ANOVA for repeated measures) was conducted to evaluate the efficiency of retrieval by group, and by repeated acquisition (1st, and 2nd).

For the purpose of serial position analysis, list items are grouped into serial position zones: primacy (items 1 to 5), intermediate (from item 6 to item 11), and recency (items 12 to 16). An analysis of variance (ANOVA for repeated measures) is applied to evaluate the probability of recall of different serial position zones (primacy, intermediate, recency) by group and by repeated acquisition.

## 3. Results

As expected, efficiency of retrieval (correct recalls minus intrusions) depends on age and presence of chronic cerebral vascular disorders (CCVD), and task sequence. Retrieval efficiency is significantly higher in younger adults (first trial M 8.8, SD 2.0; second trial M 12.6, 2.3) than in healthy older adults (first trial M 6.4, SD 2.0; second trial M 8.0, SD 2.5) across all different recall trials and retrieval efficiency is consistently and significantly higher in healthy older adults than in VCI patients (first trial M 3.8, SD 2.1; second trial M 5.2, SD 2.3) in all different recall trials (Table 1).

Younger adults benefit at a larger extent from repeated acquisition (optimal learning curve, about 50% increase after reacquisition). The older adults and the VCI patients appear to be sensitive but with a different intensity to the effects of repeated acquisition (respectively about 33% increase and 25% increase after reacquisition) (group effect: F 74.51, df 2, $p<.001$; repeated acquisition effect: F 33.13, df 2, $p<.001$).

### 3.1. Serial position analysis

The characteristics of these clinically relevant serial position effects are shown in Table 2.

Recall organization, measured as probability of recall by serial position, is consistently influenced by age and presence of CCVD (group effect: F 74.5, df 2, $p<.001$), and by repeated acquisition (F 33.1, df 2, $p<.001$).

Probability of recall for primacy zone items is different by group and by interaction between group and repeated acquisition (F 3.5, df 2, $p<.04$). Differences at the 1st immediate recall (F 15.6, df 2, $p<.001$) are dependent on age and differences due to interaction group/repeated acquisition are found for the 2nd immediate recall (F 27.5, df 2, $p<.001$). These findings suggest that the primacy effect is primarily dependent on age at the first trial; respectively younger adults (M .69, DS .18) have significantly higher scores than older adults (M .51, DS .23) and VCI patients (M .39, SD .22). Sensitivity to CCVD becomes apparent at the 2nd immediate recall when younger adults (M .89, DS .15) maintain significantly higher scores than

**Table 1**
Efficiency of retrieval by experimental groups (ANOVA, mean (SD)).

| Recall trials | Younger adults | Older adults | VCI patients | F, df 2 | p< |
|---|---|---|---|---|---|
| 1st immediate | 8.8 (2.0)[a] | 6.4 (2.0)[b] | 3.8 (2.1) | 43.8 | .001 |
| 2nd immediate | 12.6 (2.3)[a] | 8.0 (2.5)[b] | 5.2 (2.3) | 74.1 | .001 |

Means and standard deviations of number of recalled items minus the number of intrusions concerning the full list.

[a] Younger adults show significant higher scores (at least $p<.05$) than older adults and VCI patients.

[b] Older adults show statistically significant higher scores than VCI patients.