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Noile perspective  
de la nosografie  
la terapie

*„Numai schimbarea  
este statornică.”*

Schopenhauer

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# Retrogenesis in AD: evidence and implications

Liana Rada  
Borza

## Abstract

*Retrogenesis has been defined as the process by which the progression of Alzheimer's disease (AD) deterioration proceeds inversely to human ontogenic acquisition patterns. The present paper gives an overview of the functional, cognitive, neurologic, neuropathologic, neurometabolic and electrophysiological evidence that support the concept of retrogenesis. It also emphasizes a retrogenic model for detecting abuse of institutionalized people with AD. Moreover, the paper provides expert opinion on the possible ethical and forensic implications of retrogenesis.*  
**Keywords:** retrogenesis, Alzheimer's disease, ethical and forensic implications

## Rezumat

*Retrogeneza a fost definită ca procesul prin care progresia deteriorării în boala Alzheimer precede în mod invers modelul de achiziție ontogenice umane. Lucrarea de față oferă o imagine de ansamblu asupra dovezilor funcționale, cognitive, neurologice, neuropatologice, neurometabolice și electrofiziologice care sprijină conceptul de retrogeneză. Este subliniat, de asemenea, un model de retrogenic pentru detectarea abuzului identificat în cazul persoanelor instituționalizate, diagnosticate cu boala Alzheimer. Mai mult decât atât, lucrarea oferă expertize cu privire la posibilele implicații etice și medico-legale ale retrogenezei.*  
**Cuvinte-cheie:** retrogeneză, boala Alzheimer, implicații etice și medico-legale

## Definition of retrogenesis

The concept of retrogenesis has been documented as the process by which the degenerative mechanisms from Alzheimer's disease (AD) inversely recapitulate the processes of the normal neurodevelopment<sup>(1,2)</sup>.

## Functional evidence

The Functional Assessment Staging (FAST) procedure, developed from the Global Deterioration Scale (GDS) and the Brief Cognitive Rating Scale (BCRS) Axis V: Functioning and Self-Care, describes a total of 16 successive functional stages and substages in the continuum from normal aging to the late phase of AD<sup>(3,4)</sup>.

The FAST procedure clinical stages are superior to standard measures, such as the MMSE, for charting the course and assessing the severity of AD. The severe phase of AD is characterized by a GDS/FAST stage 6 in which MMSE scores begin to have floor effects, and a final seventh stage in which the MMSE is generally zero<sup>(2,5)</sup>. The sequence of functional loss outlined with the FAST appears to be a precise reversal of the order of acquisition of the same functions in the course of normal human development. Each FAST stage in AD can be described in terms of a corresponding developmental age (DA). The DA relationships to AD are very useful in the description of precise retrogenesis relationships and models in AD<sup>(2,4,6,7,8,9)</sup>.

## Cognitive evidence

The use of the modified version of the Ordinal Scales of Psychological Development – by Uzgiris & Hunt (1975) for cognitive testing in infants – has proved to be superior to the application of traditional tests, such as the MMSE, in assessing the residual cognitive capacity of subjects with moderately severe and severe AD<sup>(10)</sup>. Childhood intelligence test measures, such as the Tanaka-Binet intelligence scale (the Japanese version of the Binet scale), also proved to be useful in assessing cognition in moderate to severe AD subjects<sup>(11)</sup>.

Conversely, highly significant correlations were found between the MMSE score and chronologic age, reading age and mental age of children from 4 years onward<sup>(12)</sup>. Therefore, it was demonstrated that the MMSE, a standard AD measurement, is a suitable instrument for screening higher mental function in children at the age of 4 years and above.

## Emotional evidence

The emotional changes or the behavioral and psychological symptoms of AD are frequently similar to those experienced by infants and children at corresponding DAs. Delusions in the AD patients are very similar to fantasies in children. The so-called "delusions" in the AD patient are generally not firmly held and not fixed, frequently being only suspicions<sup>(5,6)</sup>. Moreover, stage 6 AD patients often manifest activity disturbances identical to behaviors commonly noted in children at equivalent DA (e.g. wandering away unless supervised and insistently repeated demands or questions)<sup>(6,7,13)</sup>. AD patients in FAST stages 5 and 6 also develop many of the same anxieties and fears as children of equivalent DAs<sup>(14)</sup>.

## Neurologic evidence

Many of the same developmental reflexes that mark the transition from normal infancy to early childhood appear to be equally robust markers of the entry into the "infantile" stage of AD. In this regard, it was shown that the emergence of the tactile sucking reflex, palmar and plantar grasp reflexes, the Babinski reflex distinguished the "infantile" stage of AD from the "early childhood" stage of AD with a specificity, sensitivity and overall accuracy each greater than 85%. Thus, at the AD stages corresponding to DAs at which developmental reflexes are frequently manifest, these primitive reflexes occurred in the great majority of patients<sup>(1,2,15)</sup>.

## Neuropathologic evidence

The process of myelin loss, which is associated with the retrogenic process occurring in AD, has been termed "arbo-

real entropy”, as follows: “Just as the bark of a tree protects it from external injury, and, to some extent, the thicker the bark, the greater the protection, the myelin protects the axon and its neuron. Hence, to some extent, we may say the thicker the myelin, the greater the protection.” Consequently, the developmentally most recent, thinly myelinated, brain regions are the most vulnerable to AD pathology<sup>(1,7)</sup>. The pattern of neurofibrillary changes which gradually develops in the course of AD bears a striking resemblance to the inverse sequence of cortical myelination in normal development<sup>(16)</sup>.

## Neurometabolic evidence

A leading investigator in neurometabolism noted the similarities between the pattern of neurometabolism in normal infant brain and the pattern of neurometabolic deficit in late-stage AD brain. Both the infant and the AD patterns of neurometabolic activity are markedly different from that of the normal aged adult<sup>(17,18)</sup>. Moreover, the regions of the brain which were most metabolically active in the default (awake, resting) states in young adults proved to be the most vulnerable to the AD pathology, as the pattern of amyloid deposition appeared to occur in these regions in older adults with AD<sup>(19)</sup>.

## Electrophysiological evidence

In AD there is a progressive decrease in fast wave (alpha and beta) activity and a parallel progressive increase in slow wave (delta and theta) activity, the converse of what occurs in normal development. Specifically, it has been found that there is no statistically significant difference in delta, theta, alpha and beta activity between the stages of AD and their corresponding age groups in normal development<sup>(20)</sup>.

## A retrogenic model for detecting abuse of people with AD

It has been shown that the adapted and extended version of an instrument that would ordinarily be used in detecting

maltreatment in childhood and adolescence can be efficiently used as an abuse screening tool in AD people living in institutional settings, providing new evidence for the practical utility of the concept of retrogenesis. Thus, the 38-item adapted Child Abuse and Trauma Scale (CATS) – initially developed by Sanders and Becker-Lausen (1995) – appears to be a unified construct that reliably measures the multidimensional nature of the abusive experiences lived by institutionalized AD persons<sup>(21)</sup>.

## Ethical and forensic implications

An expert opinion survey conducted in 2010 in Iași draws attention, for the first time, to possible ethical and forensic implications of retrogenesis. The majority of experts questioned in this survey considered it ethical to start from the concept of retrogenesis when approaching AD. Most of the survey participants agreed that it would be ethical to use psychometric tests and programs of cognitive stimulation originally developed for the child in the person with AD. More than half of the professionals considered it ethical to apply child abuse evaluation tests to the AD persons. 61.2% of the opinion survey respondents agreed that it would be necessary to use the concept of retrogenesis for assessing mental capacity in these patients. Most professionals surveyed herein pointed out that it would be necessary to enact legislative proposals on the protection of the AD person, which would be adapted after the model of the current child protection legislation<sup>(22)</sup>.

## Conclusions

In conclusion, several studies provide strong evidence for this degenerative developmental recapitulation termed retrogenesis. The present findings may have humanitarian implications for persons with AD and may, hopefully, reduce the stigma and burden associated with this medical condition. ■

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