

Basis Of The Psycho Social Crisis And Sensory Recognition System Blockade Theory For Alzheimer's Disease

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Abstract

Behavioral and sensorial deficits were frequently reported associated with Alzheimer's illness. We determine predictive power, sensibility and specificity of sensorial deficits and deficient behavior factors in the areas Functionality, Behavioral social relations, Affective net, Abstract entity's dynamism, Coping deficit of personal losses, Vital motivation, Interest and initiative, and Sensorial perception disposition.

A prospective longitudinal study was followed with a cohort of 237 cases both gender Mild Cognitive Impairment's cases and after were rigorously screened to ensure they did nor meet criteria for dementia in comparison of. social active healthy elders. Both groups were followed during six years and a diagnostic evaluation for Alzheimer's disease determined at the end of two years. Statistical regression logistic analysis was applied with de SPSS 10.0. Deficient behavior factors in different areas appear with different power predictive values in the order sensorial perception deficit, coping deficit of personal losses, apathy, affective isolation, de-motivation, introversion, poor dynamism with abstract entities, some kind of depression and secondary status/dependence/exclusion/auto-exclusion. The sensorial recognition deficit appears as the strong predictive factor. All factors can be cluster under the idea of a personal active isolation and coherent with this way voluntary recognition deficits contribute to produce synapse disruption, neuronal death and the corresponding neural nets progressive disintegration.

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INTRODUCTION

Several non biological factors were reported in the last 25 years, like social and personal behaviors, cultural, economics and educative factors that seems associated with the process named Alzheimer

(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40), obtained by means of the application of epidemiologic methodology. Nevertheless, some results seem contradictory, but actually now a large number of factors appear as clearly associated with Alzheimer and its counterparts as protective:

Figure 1

Low schooling in developed countries	High schooling in developed countries, not in undeveloped ones
Personal low income in developed countries, not in undeveloped ones	High dynamism with abstract entities in undeveloped countries
Manual labor in developed countries	Intellectual labor in developed countries, not in undeveloped ones
Labor performance with low socialization	Labor performance with high socialization in undeveloped countries
Weak social relations	High frequency and plural social relations
Urban cultures. Quite structural industrial society. Isolated rural culture.	Rural culture with satisfactory familial productivity
Isolation, introversion, enclosure	Active life
Coping deficit of personal losses	Strong or normal coping of personal losses
Weak affective net	Important affective net
Belong to a weak social net	Belong to an important social net
Pertenecer a una red social débil	Pertenecer a una red social importante

Other social and familial factors had been reported last time, but yet remains uncertain, as for example pair status, family low income, introversion familial behaviors, and others.

Conde-Sala (41) report recently the father death before the twenties as a possible new risk factor, and we also meet with several cases of several painful losses that occurred 30 or 50 years ago, and at present revival in coincidence of an at

present another loss.

All these studies were carried out under epidemiological methods that are quite useful to determine circumstances, scenarios and factors that can be associated to the problem, but doesn't establish causalities.

These methods also are applied to biological factors like gene alleles, toxics and chemical contaminants, and subject to the same uncertain causalities.

Moreover, the well known and frequent studies on brain tau and amiloid proteins also are epidemiologic and not experimental ones, and always happened that there are persons with Alzheimer and without these proteins and vice verse, or more recently, there are persons with Alzheimer and without other gene alleles claimed as risk factors (yet more than 300 at present) and vice verse.

Something like that occur with level of education and Alzheimer's risk: most of the elderly in developed countries with an education's high schooling appear as having a low risk for Alzheimer, but there are persons with Alzheimer that had reach a high schooling, as a Nobel prize, for example.

At present the entire hypothesis about the genetic or anatomy pathologic origin of the Alzheimer's process are controversial in order to different facts.

Yet the modern genetic theory remains valid in spite of several revisions made to try adjust the gene hypothesis in Alzheimer's process, like that a gene can be expressed at the forty or at the ninety, or the existence of a universal lethal gene, or that a gene can be present and isn't expressed, or vice verse, that can be absent and expressed, or that a gene can be a risk factor without knowing nothing about the logic justification for it, and that nothing of these new contribution to genetic theory occur in plants and animals except in particular and comprehensive cases in embryologic and development phases.

Moreover, putting this gene in a mouse (transgenic mouse), protein tau is produced but not a dementia like state (68).

This takes to think about a fundamental participation of the non biological factors in the installation of this type of dementia, in addition to the reports of good results that give psychological and psychiatric treatments in its early phases (61,62,63,64).

The weak capacity to determine causalities in epidemiologic

research can improve something determining the predictive power of the different factors and this can be obtained with longitudinal prospective studies of cohort, to which it is applied statistical techniques of logistic regression. And this it has been the method followed in the present investigation.

SUBJECTS AND METHODS

The study has been made from the university data base created in 1994 for epidemiologic multi factorial studies of elderly dwelling in the media river basin of the Uruguay River (Uruguay, Argentina and Brazil).

From this were selected 237 individuals (Women 67,5%, Average age 74.4 years), with previous clinical history of Mild Cognitive Impairment but without dementia, and followed in different groups during six years from 1994 to 2005 in three steps of two years.

Also other so many greater adults with normal aging were included in the study belonging to diverse social groups like retirements and pensioned, groups of dance and folk, European origin's collectivities associations, and others.

Both groups were followed during six years applying a protocol directly or with the help to their relatives or most near caregivers to evaluate the different factors as in previous studies (34, 35), and applying also the simple home sense tests that were described later.

Those evaluated in this protocol is around the factors that have the same intrinsic logic keys like restriction, isolation, inactivity, disaffected and so on, according to our abduction conception of active isolation or encapsulation for the installation of this type of dementia. Also in some cases were probed as associated to Alzheimer's illness by diverse previous investigations of different groups in diverse countries.

The protocol evaluates eight areas: Functionality, Behavior of social entailment, Affective net, Dynamics of relation with abstract entities, Coping of personal losses, Vital motivation, Interest and initiative and Perceptive sensorial disposition.

The deficit variants of these areas were enunciated respectively as the followings: [Some form of depression] and [Secondary status, dependency, exclusion, auto exclusion] for Functionality, [Social introversion] for Behavior of social entailment, [Affective isolation], for Affective net, [Weak or null relation with abstract

organizations] for Dynamics of relation with abstract entities, [Coping deficit of personal losses] for Coping of personal Losses, [De-motivation] for Vital Motivation, [Apathy] for Interest and initiative, and [Perceptive sensorial blockade] for Perceptive sensorial disposition.

This last variable would correspond with inhibition in the studies of attentional modulation and that is expressed by components of identification sense's deficits

($42 \times 43 \times 44 \times 45 \times 46 \times 47 \times 48 \times 49 \times 50 \times 51 \times 52 \times 53 \times 54 \times 55 \times 56 \times 57 \times 58 \times 59 \times 60 \times 61$), or in other language attention-dependent and attention-independent responses ($65 \times 66 \times 67$).

The functionality represents the basic nucleus of modality of affective and social entailment and to the auto construction, and their deficit forms are enunciated as [some form of depression], on the one hand, and [secondary status, dependency, exclusion or auto exclusion], on the other, what is equivalent to the lack of any protagonist role in the social and familial relations and [social introversion] is defined as relations restricted to the home or with few relatives, and also in the labor relations, or to belong to restricted circles, and have little or null social exploration, [affective isolation] is the condition enunciated by the own person like not being wanted or being loved by anybody and in addition by a lack of containment with regard to a personal crisis.[Little or null relation with the abstract entities] is equivalent to the condition of not exerting the reading, not to follow the news in any format, not to write, not to express itself artistic or as an artisan, only to see games and banal programs by the television, [Coping deficit] like the incapacity to generate a positive alternative forehead to a personal loss, [de motivation] like the absence of initiative to obtain a new personal objective by a given way and in addition to have limited affective answers facing positive or negative situations, [Apathy] like the absence of reaction as opposed to weak or normal stimuli, and finally [sensorial perceptive blockade] is the lack of answer facing to stimuli in the senses that demand any identification (recognition) of it.

The senses of the vision, hearing, smell, touch and taste were proved with a simple at home test to detect fault of identification central capacity but sustained peripheral reactive capacity.

Vision was tested offering a well-known relative's picture (no response), and the attention independent component by a way a strong flash of light (response); auditory function

speaking normally (no response) and then with a strong auditory signal (response); taste offering a piece of sweet fruit jelly and immediately a neutral jelly (no response), and then a piece of wormwood (response), smell offering their preferred perfume (no response) and then a piridin vapor (response) and tactile by soft touching the hands and then with a cold air on one hand. The sense of the equilibrium, body perception and the space location can not be proved satisfactorily yet. A sensorial perceptive blockade is standpoint when at least three senses were affected.

At the end of every period of two years both groups were examined to make the clinical diagnosis and application of criteria NINCDS/ADRDA for Alzheimer by a geriatric physician and neurologist specialized in dementias in the elderly.

Data analysis: Inferential statistics and modelization analysis was performed with of SPSS v. 10.0 Windows program. Before introducing the nine factors in the model the multi co linearity was examined.

RESULTS

Table 1. Demographic profile of both groups of participants, with Mild Cognitive Impairment non Dementia (MCInoD) and Normal Aging ones (NA). Average and standard deviation.

Figure 2

Table 1: Demographic profiles of both groups of participants, one with Mild Cognitive Impairment no Dementia (MCInoD) and Normal Aging (NA)

	MCInoD	NA	
Media and SD years old	72,67 (10,7)	74,1 (12,9)	
Schooling	6,9 (10,0)	6,7 (8,5)	
Familial income	300U\$±60%	300U\$±60%	
Women	67,5%	67,5%	
MMSE	23,2 (0,99)	28,4(1,6)	p< 0,000

The MANOVA analysis determined a η^2 effect (Wilks) of 0.79 with F of 12,01 and $p < 0,001$. At level of all the considered factors separately, the groups differed only in the MMSE

At the end of each stage the number of cases of both groups diagnosed with Alzheimer appears in Table 2.

Figure 3

Table 2: Number of persons with the factor/number of Alzheimer's case at the end of each step/number of initial cases in the follow up.

factor	FIRST STEP		SECOND STEP		THIRD STEP	
	MCI's group	Normal ageing group	MCI's group	Normal ageing group	MCI's group	Normal ageing group
Some type of depression	19/44/237	2/2/237	25/48/217	1/2/214	20/49/190	2/3/210
Secondary status, dependence, exclusion, auto exclusion	19/44/237	0/2/237	24/48/216	0/2/216	23/49/194	0/3/209
Social introversion	22/44/237	2/2/237	27/46/217	2/2/217	29/48/186	2/3/212
Weak or null relations with abstract entities	31/44/237	0/3/237	37/46/216	0/2/221	30/48/186	0/3/211
Affective isolation	29/44/237	1/3/237	36/46/216	1/2/219	39/49/186	1/3/210
Coping deficit of personal loss	31/45/237	2/2/237	34/47/217	2/2/220	28/50/187	2/3/213
Apathy	27/43/237	0/2/235	27/42/212	0/2/217	24/49/185	2/3/209
De-motivation	31/44/237	0/2/237	28/42/219	0/2/214	29/51/185	1/3/210
Sensorial perceptive blockade	39/45/214	0/2/237	39/48/218	0/2/216	45/49/190	0/3/211

Note: Deaths, illness or disease and lost of contact with cases explain the little variations in reference initial cases and controls.

Under a categorization Alzheimer versus dementia a logistic regression analysis were performed in order to evaluate behavior's factors power in predicting the dementia of Alzheimer type. In this analysis the age, genre, schooling, familial income and MMSE's values were controlled in the model, and only this last appeared with significant differences.

The relative importance of the different factors has been evaluated by logistic regression.

Figure 4

Table 3: Behavior factors, Sensorial perception blockade, MMSE and Alzheimer's prediction by logistic regression analysis.

Factores	β	OR	95% IC	p
Some type of depression	0,73	2,62	1,82-2,95	0,01
Secondary status, dependence exclusion, auto exclusion	0,59	1,82	1,24-2,05	0,1
Social introversion	0,77	3,28	1,77-5,53	0,001
Coping deficit of personal losses	0,82	3,39	1,86-6,74	0,002
Weak or null relations with abstract entities	0,77	3,11	1,77-6,91	0,001
Affective isolation	0,94	4,576	2,56-6,99	< 0,001
Apathy	0,92	4,549	2,31-7,79	0,001
De-motivation	0,94	4,47	2,44-6,69	0,001
Perceptive sensorial blockade	1,57	6,99	4,99-8,75	< 0,001
MMSE	0,74	2,66	1,78-3,47	0,01

Nota: β regression coefficient; OR, odds ratio; IC, confidence interval; MMSE, Mini Mental State Examination.

The cases of Alzheimer were codified like 1 and the normal ones like 2. The variables entered as a block and are

continua in the metric one of z values. The Odds Ratio represents the relative risk of incidence of dementia with independence of the other factors in the model.

As is usual, in order to quantify the importance of the additional measures in the prediction of the dementia incidence, sensitivity, specificity and the corresponding predictive values were calculated for each behavior factor. Sensitivity represents the proportion of people with dementia by accurate clinical diagnosis to those who the logistic regression equation classifies like with dementia, whereas the specificity is the proportion of people without dementia by accurate clinical diagnosis to those who the procedure describes like without dementia.

The different values were transformed to z values to maintain the same metric between factors, in order to facilitate the comparison. The regression coefficient indicates that the individuals that have high values are more prone to Alzheimer's dementia. In a parallel statistical process these factors do not appear as independent (with other one, or other two, etc.) and in last instance can be considered as all bound, a random coincidence with the supposed reality.

Figure 5

Table 4: Sensibility, specificity and Positive and Negative predictive values estimated by way of the logistic regression analysis.

Factor	Predictive values			
	Sensitivity	Specificity	Positive	Negative
Some form of depression	0,58	0,72	0,69	0,77
Secondary status, dependence, exclusion, auto exclusion	0,55	0,62	0,63	0,72
MMSE	0,62	0,78	0,71	0,79
Social introversion	0,70	0,90	0,84	0,92
Coping deficit of personal losses	0,85	0,95	0,88	0,95
Weak or null relations with abstract entities	0,60	0,74	0,77	0,83
Affective isolation	0,83	0,93	0,85	0,95
Apathy	0,78	0,90	0,88	0,94
De-motivation	0,80	0,88	0,84	0,93
Sensorial perception blockade ¹	0,95	0,97	0,96	0,98

¹ Recognition failure

CONCLUSION

The behavior factors considered here, notably the perceptive sensorial blockade, have more or less predictive power. Both [Some kind of depression] and [Secondary status,

dependence, exclusion, auto exclusion] alone can be said that don't have a predictive power. In the other extreme it can be said that the sensorial deficits is the morning call or diana of the beginning of the irreversible phase of the process, and it in spite of its fluctuating expression and well known dependence on the emotional condition of the person. Another important conclusion is that the different factors they are not fragmented in the process of logistic regression, but that keeps interdependence in the different possible combinations, although conceptually they correspond to quite different entities in the reality.

Nevertheless these results, the deficits in the senses in Alzheimer's cases that have been reported for more than two decades, always they have been taken like only as an epiphenomenon of dementia, and not a key question.

Only recently has been established that the deficits are in the identification or recognition component of senses, and that the corresponding peripheral reactive components remains without affecting until reach to the last phases of the process. Diverse authors agree in which these deficits can be used for a precocious detection of Alzheimer, and is intended now to develop an accessible at home test battery that it would be very important to anticipated professional actions.

The deficits take place in the diverse senses, reason by which it can be presumed that respond to interference in a general regulatory mechanism, that it can well be the attention-dependent and attention-independent mechanism (65,66,67) of the attentional modulation, to which all we resorted daily to modulate the excesses of stimuli in the directions that haven't interest for us.

DISCUSSION

The psico social sensorial recognition neuronal disintegration theory of Alzheimer

The active isolation or capsulation idea has arisen by way of detect a temporarily sequential of the different behavior factors, not only those studied here considered but others also reported from several research groups. By means of a semiotic analysis it has arisen that the concept of active isolation or capsulation can be the goal concept that includes to all those factors, like secondary status, dependence, exclusion or auto exclusion, in order to follow by some type of depression, introversion, affective isolation, weak social network, poor relation with abstract entities, apathy, demotivation, and culminating in the blockade of the

identification components of senses by way of an extremist shut off of the attentional modulation concluding in a strong recognition failure.

Elementary logic indicates that whom carrier the appropriate language in and out the brains is indeed the senses, because understand and participate in the neuronal networks of the brain, and because have the necessary words: electrical and chemical words in the corresponding way of transmission. All seems like that sense deficits goes to synapse disruption in the recognition neural system and then disrupt the entire neuronal net and as a consequence its brain function breakdown expression.

In such a manner this locates this type of dementia within already more than a centennial alternative paradigm that it establishes that there is a way to tie with painful facts of our past and also a peculiar way to tie with the present reality, that it can get to alter so deeply our relations with the world that even affect as far as destroy a healthy brain.

Under the model proposed in this paper it's possible to explain the influence of retirement plus marginalization in the elderly, why the population prevalence are greater in urban cultures than in satisfactory stable rural ones, why until now all the hypothesis of genetic, anatomic or organic basis have failed, why the psychiatric or psychological interventions acts successfully in the early phases, why some biochemical and histo-pathological findings are compatible with this model, since they can well be epiphenomenon of the progressive neuronal death, the dissolution of the neuronal networks and the interruption for long time of its normal function on the brain, why it can be happen as much in the young adult as in the very greater adult, why the powerful plural affective nets have a protective effect, why belonging to maintained networks of socialization has also so much such protective power, and so on.

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