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✦ Case series

REELIN-COLBOS (H3447R) in Colombian oldest-old individuals, a case series

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Abstract

We previously identified *REELIN*-COLBOS (*RELN* H3447R) and *APOE* Christchurch (*APOE* R136S) as candidate gene variants associated with protection against dementia in cases at the highest risk of Alzheimer's Disease (AD) due to the *PSEN1* E280A mutation in Colombia. Here, we examined the frequency of these variants in a cohort of 135 Colombian oldest-old individuals, part of the Resist AD Project. Five carriers of the *REELIN*-COLBOS variant were identified and described here, whereas none of the cases carried *APOE* Christchurch. The first case is a 102-year-old APOE4/E3 carrier with stable performance on cognitive tests despite having suffered an episode of delirium due to pneumonia. FDG-PET revealed relatively preserved cortical glucose metabolism despite showing degenerative changes on MRI. Another case with a family history of early-onset dementia maintained independence until age 85. Despite significant comorbidities, the

other three cases exhibited preserved cognition at baseline. These observations are consistent with the hypothesis that the Reelin-COLBOS variant may play a protective role against cognitive decline and support healthy aging, although further studies are needed in larger and more diverse populations to confirm this association.

Introduction

The global rise in life expectancy has intensified interest in uncovering the factors that promote longevity and healthy aging. While numerous environmental and lifestyle influences have been implicated in the aging process (1), the existence of exceptionally long-lived individuals who remain cognitively unimpaired despite comorbidities has brought attention to less evident contributors, particularly genetic factors (2). Aging well often requires delaying the onset of age-related changes and avoiding potentially fatal conditions, such as external injuries, metabolic and vascular diseases, cancer, and neurodegenerative disorders (3).

The Neuroscience Group of Antioquia (*Grupo de Neurociencias de Antioquia, GNA*) has previously identified two individuals with genetic protection against Autosomal Dominant Alzheimer's Disease (ADAD) caused by the Presenilin-1 (*PSEN1*) E280A variant. One was a woman who had a nearly 30-year delay in disease onset, attributed to homozygosity for the *APOE3*-Christchurch variant (*APOE*-R136S, APOE3Ch) (4). The other case was a man who remained cognitively intact until age 67 and carried a heterozygous Reelin variant (*RELN*-H3447R), now referred to as *REELIN*-COLBOS in recognition of the Colombia-Boston biomarker collaboration. These cases have spurred interest in identifying additional genetic variants that may confer resilience to Alzheimer's disease.

Building on these findings, the GNA initiated a study of individuals over the age of 80 to identify potential protective factors against cognitive decline and dementia at the oldest ages, entitled "Resilience to Cognitive Decline and Resistance to Alzheimer's Disease and Related Neurodegenerative Disorders in Colombian Individuals with Autosomal Dominant Dementias". In this cohort, we examined the distribution of gene variants previously linked to resilience and identified five carriers of *REELIN*-COLBOS. The presence of this variant at an allelic frequency markedly higher than that estimated for the Latin American population raises the question of a potential association with longevity and the underlying biological mechanisms involved. In this report, we describe the clinical profiles of these cases with particular emphasis on cognitive status and comorbidities.

Methods

Participants were drawn from a cohort of 135 individuals aged 80 years and older enrolled in the ongoing Resist AD Project, based on broad inclusion criteria: being over 80 years of age, recognized by family members for either preserved cognitive functioning or exceptional longevity. Priority was given to the oldest identified cases through snowball sampling. As part of the study protocol, all participants underwent blood sampling for future biomarker studies and comprehensive medical and neuropsychological evaluations, either at the clinic or in their homes, depending on their ability to travel. All participants were screened for the presence of

REELIN-COLBOS, *PSEN*1-E280A, APOE2, APOE4, and APOECh variants (see Allelic frequencies in Supplementary Table 1). Sequencing methods are explained below.

Medical assessments were conducted by dementia-trained physicians using semi-structured interviews, while neuropsychological evaluations employed Spanish-validated instruments, the CERAD neuropsychological battery test adapted to the Colombian population (5), Yesavage's geriatric depression screening scale, the 7-items Generalized Anxiety Scale (GAD-7), the Functional Assessment Staging scale (FAST), the patient and caregiver complaints scale, the Lawton & Brody functional assessment scale, and the Barthel Index. When feasible, participants also underwent structural MRI and 18F-fluorodeoxyglucose (FDG) PET imaging at Hospital Pablo Tobón Uribe in Medellín, Colombia (only available in one of these five cases). Average FDG-PET signal z-scores were calculated for 34 bilateral cortical regions parcellated using the Desikan–Killiany atlas from Freesurfer, which comprises 13 frontal, 7 parietal, 9 temporal, 4 occipital regions, and the insula. The reference group included data from 39 middle-age cognitively normal individuals from the same region in Colombia. For each brain lobe, the proportion of regions with preserved metabolism (z-score>−1.96) was then computed.

Genomic DNA (gDNA) was extracted from patient blood samples at the GNA. SNP genotyping was performed through PCR amplification and Sanger sequencing, outsourced to GENEWIZ (Azenta Life Sciences) as a fee-for-service. DNA samples were quantified and prepared following GENEWIZ guidelines (600 ng per sample at 20 ng/µL). Custom primers were designed by GENEWIZ based on the provided SNP IDs (Supplementary Table 1), followed by PCR amplification and sequencing. Raw sequencing data were analyzed using ApE (A Plasmid Editor) for SNP visualization and genotype interpretation.

The original project received approval from the Institutional Ethics Committee of the University of Antioquia, Medellín, Colombia. All participants—or their legally authorized representatives when applicable—provided written informed consent before enrollment.

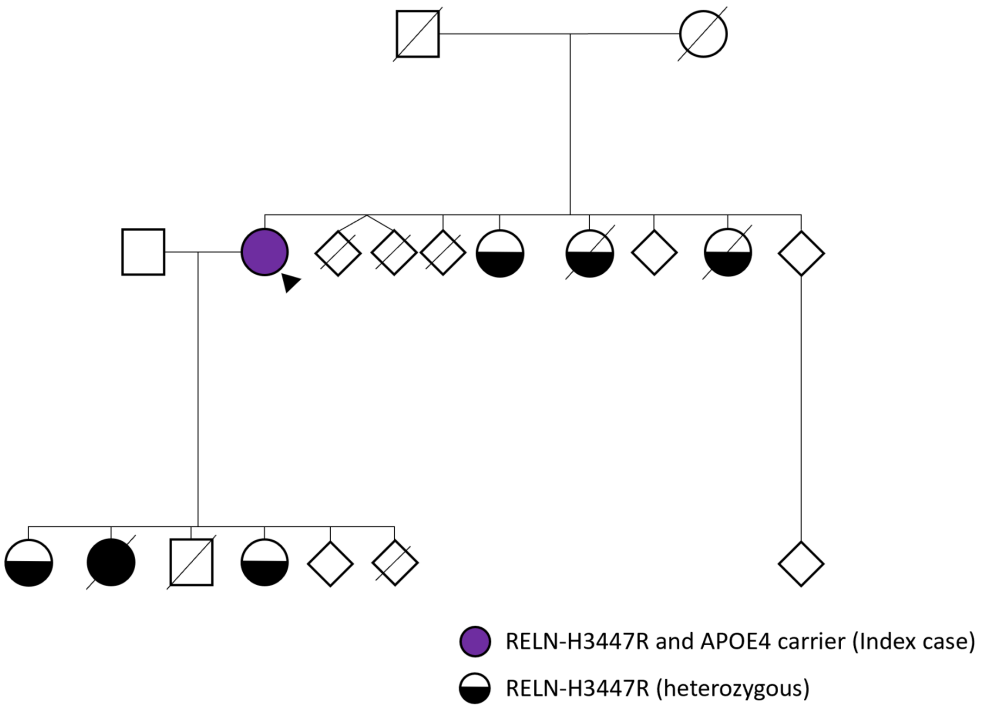
Results

Cohort characteristics

The cohort had 135 individuals (73% females) with a mean age of 92 ± 6.6 (52% aged between 90-99 years and 21% with more than 99 years).

Genetic analysis showed that the distribution of APOE alleles was consistent with that of the general population (6). As expected, no carriers of the *PSEN1* E280A variant were identified. The APOE3 Christchurch variant was also not detected in this cohort. Notably, five individuals—among them some of the oldest participants—were found to carry the *REELIN*-COLBOS variant, raising the possibility that this rare variant may contribute to cognitive resilience and exceptional longevity (Supplementary Table 1).

Figure 1. Genealogy of the index case specified based on the *REELIN*-COLBOS status. The purple circle represents the index case, who is a carrier of *RELN*-H3447R and APOE4. The black-and-white circle denotes individuals heterozygous for *RELN*-H3447R, while the black circle represents those homozygous for *RELN*-H3447R.



Case #1 (*RELN*-H3447R and APOE4/3)

A woman with three years of formal education and three *REELIN*-COLBOS carrier siblings (Fig.1) underwent her first clinical assessment at the age of 102. Her medical history included passive smoking for 10 years, hypertension, dyslipidemia, left hip fracture, hearing loss, and knee osteoarthritis. She was taking multiple medications, including memantine (10 mg daily), and fluoxetine (20 mg daily). At 102, she reported two years of memory complaints, difficulty focusing, and disorientation in time and place, but remained independent in basic daily activities- ADLs (FAST=4, MMSE=17). MRI showed cortical atrophy, periventricular leukoaraiosis, and a right cerebellar lacunae (Fig.2a); FDG-PET demonstrated relatively preserved cortical glucose metabolism, primarily within the frontal (8/13 regions; 61.54%), parietal (4/7; 57.17%), and temporal (4/9; 44.44%) lobes, as well as in the insula, while all four occipital regions exhibited significant hypometabolism compared with middle-aged (39.56±6.68 years) cognitively normal individuals of the same kindred (Fig.2b). Seven months later, she showed worsening spatial disorientation, verbal fluency, behavioral changes, and partial dependence in ADLs (FAST=6, MMSE=15), but by age 104, her behavior and function improved, with stable memory and language performance (FAST=4, MMSE=15). The patient was still alive in January 2025 at the age of 105.

Figure 2. Index case neuroimages MRI and PET-FDG at the age of 102. 2A) Brain MRI at 102 years with generalized involutional changes and the findings described in the text are shown in each figure. Upper left: Multiple leukoaraiosis in the periventricular white matter. Upper right: Signs of old lacunar infarction in the right cerebellar hemisphere. Bottom left: Increased sulcus depth with compensatory ventricular dilatation. Bottom right: Thinning of the corpus callosum. 2B) Bilateral medial cortical surface views showing relatively preserved frontoparietal metabolism as measured by FDG-PET. The color scale indicates FDG SUVr values, with blue representing the lowest values and red representing the highest values (range: 0.5–1.8).

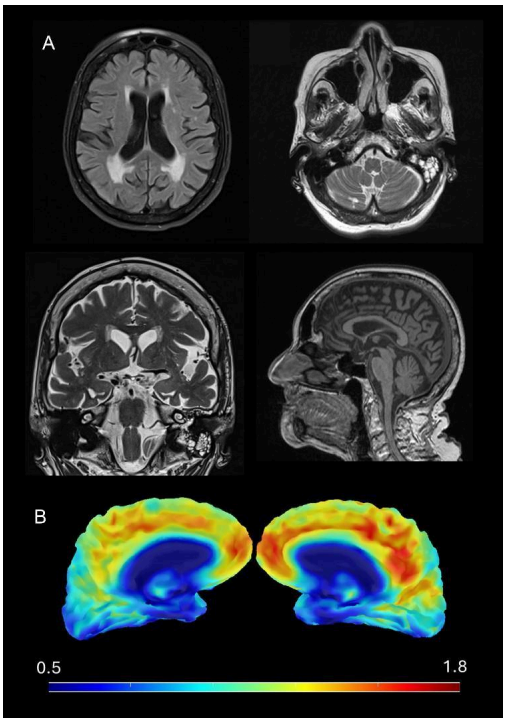


Table 1. Neuropsychological follow-up of the Index case (Case #1).

		102 yr.	102 yr. + 7 mo.	104 yr.
		Score (Z)	Score (Z)	Score (Z)
Global	MMSE /30	17 (-3.5)	15 (-4.3)	15 (-4.3)
Language	Semantic Fluency- Animals	7 (-1.2)	5 (-1.7)	7 (-1.2)
Memory (verbal)	CERAD Word List Learning Total Score /30	5 (-2.2)	7 (-1.6)	5 (-2.2)
	CERAD Word List Learning Recall /10	0 (-1.8)	0 (-1.8)	0 (-1.8)
	CERAD Word List Learning Recognition /10	5 (-1.5)	1 (-3.7)	2 (-3.1)
Memory (visual)	CERAD Constructional Praxis Recall /11	0 (-1.2)	0 (-1.2)	0 (-1.2)
Perceptual -motor	CERAD Constructional Praxis Copy /11	5 (-0.7)	7 (0.3)	4 (-1.2)
Executive	Phonemic Fluency- F-A-S	7 (-1.6)	2 (-2.1)	0 (-2.2)

CERAD = Consortium to Establish a Registry for Alzheimer's Disease; MMSE = Mini-Mental State Examination; NA = not applicable/missing; Z = Z-score.

Case #2 (*RELN*-H3447R and APOE2/3)

A woman with no formal education who worked as a housewife and waitress presented with a complex medical history, including hyperacusis, osteoporosis, unilateral blindness from retinal detachment, cerebral aneurysm surgeries, and a right knee prosthesis. She smoked lightly for 10 years and cooked with wood and charcoal. Her medications included omeprazole (20 mg daily) and acetaminophen (500 mg q8h). Memory complaints began at age 80. At 82, she was fully independent with normal cognitive performance (FAST=2, MMSE=29). By age 85, despite increased memory concerns and a lower MMSE (MMSE=22), she remained functionally independent in daily tasks. She died at the age of 86 due to COVID-19 complications.

Case #3 (*RELN*-H3447R, APOE3/3)

A woman with three years of education and multiple chronic conditions—including insulin-dependent diabetes since age 91, oxygen-dependent COPD since 86, hypothyroidism, hypercholesterolemia, arterial hypertension, heart failure, and epilepsy—had a history of heavy smoking and cooking with firewood. Despite her medical burden, she remained cognitively intact and independent at age 91 (FAST=1, MMSE=30). By age 94, she showed signs of mild dementia (FAST/EDG=4, MMSE=20), which progressed to moderate-severe dementia by age 98 (FAST=6, MMSE=12). She was taking multiple medications, including metformin (850 mg daily), insulin glargine 20 IU daily, and levothyroxine (50 mcg daily). Her family history included several long-lived, cognitively healthy relatives. She died at the age of 98 due to complications from a stroke.

Case #4 (*RELN*-H3447R, APOE3/3)

A woman with four years of education, six children, and a history of hypertension, scoliosis, and dyslipidemia managed with multiple medications, including atorvastatin (40 mg daily) and furosemide (40 mg daily). She was exposed to firewood smoke for a decade and had no family history of neurodegenerative disease. Cognitively stable at 82 (FAST=1, MMSE=28), she developed mild dementia by age 93 (FAST=4, MMSE=16). She died at the age of 95 due to “senility”.

Case #5 (*RELN*-H3447R, APOE3/3)

A woman with five years of education, three daughters, and a complex medical history—including hypothyroidism, hypertension, diabetes, breast cancer (in remission), hearing loss, and transient ischemic attacks. She was taking multiple medications, including levothyroxine (100 mg daily), furosemide (40 mg daily), insulin glargine 34 IU every morning, and loratadine (10 mg daily). She had a history of smoking and firewood exposure and no known family history of neurodegenerative disease. At age 90, she presented with time disorientation and mild cognitive impairment (FAST=3, MMSE=19) but remained functionally independent. MRI showed right M1 stenosis and severe

microangiopathy. Visual testing was limited due to macular degeneration, though verbal cognitive performance was within the expected range. She died at the age of 92 due to complications from a stroke. Neuropsychological follow-up of cases 2-5 and clinical/functional scales are shown in Supplementary Tables 2-4.

Discussion

Among 135 individuals from a cohort of Colombia's oldest-old, we identified five carriers of the *REELIN*-COLBOS (H3447R) variant who exhibited relatively preserved cognitive function at baseline. This corresponds to an allele frequency of 1.9%, which is 380 times higher than that reported for the general Latin American population (0.005%) and markedly exceeds global estimates of 0.000008 (1 in 125,000), with enrichment in admixed American populations reaching 0.00005 (1 in 20,000) (7). Given the broad polymorphic landscape of the RELN gene, the presence of *REELIN*-COLBOS in this cognitively resilient group of oldest old individuals aging well raises questions and hypotheses about a potential association between this variant, longevity, and protection against cognitive decline.

The REELIN gene encodes an extracellular matrix glycoprotein characterized by distinct structural domains, which in the adult brain is predominantly expressed in GABAergic interneurons located in the cortex, hippocampus, entorhinal cortex, and cerebellum (8,9). Additionally, it promotes the morphological maturation and dendritic spine development of newly generated neurons (10).

Reelin has traditionally been attributed a high binding affinity for Apolipoprotein E Receptor 2 (ApoER2/LRP8) and Very Low-Density Lipoprotein Receptor (VLDLR). Upon ligand binding, these receptors recruit and phosphorylate Disabled-1 (Dab1), which in turn activates multiple downstream signaling pathways, including the PI3K/Akt pathway, which promotes cell survival and metabolic regulation; the Crk-C3G-Rap1 axis, involved in integrin activation and cell adhesion; GSK3β inhibition, potentially leading to reduced tau hyperphosphorylation; and Src/Fyn kinase-mediated enhancement of NMDA receptor (NMDAR) signaling, which may facilitate synaptic transmission (11–13).

Thus, age-related reductions in the density of Reelin-expressing neurons have been documented in human, primate, and murine models, with entorhinal cortex decline specifically associated with cognitive deterioration in rats (14,15). This neuronal loss, together with in situ proteolytic processing and misfolding of Reelin proteins, has been implicated in the accumulation of hippocampal oligomers, which correlate with astrogliosis, reduced bioavailability of soluble Reelin, limiting receptor activation, and facilitation of amyloidogenic processes, as Reelin deposits have been shown to colocalize with Aβ plaques (16). Furthermore, Reelin depletion during aging may compromise NMDAR-dependent synaptic plasticity, thereby reducing long-term potentiation capacity and impairing learning and memory (14).

Regarding the variant in our cases, *REELIN*-COLBOS is a gain-of-function variant originally reported in a man with the *PSEN1*-E280A mutation who remained cognitively unimpaired until age 67, nearly three decades beyond the expected onset of Alzheimer's

disease (17). Other *RELN* variants have been linked to reduced AD neuropathology in cognitively unimpaired elderly (rs4298437, rs6951875, rs6943822), further supporting its protective effect (18).

Considering that reaching the oldest-old stage has significant challenges due to numerous genetic, environmental, and health-related risks to longevity and cognition, we hypothesize that the *REELIN*-COLBOS variant may have an impact through different protective pathways.

Thus, we hypothesize that *REELIN*-COLBOS was able to at least partially offset the metabolic and cognitive decline risk conferred by the APOE4 allele (19,20) in CASE #1. Mechanistically, *REELIN*-COLBOS enhances binding to ApoER2/LRP8 and VLDLR, outcompeting APOE4. This interaction activates the Reelin signaling pathway, which activates Dab1, inhibits GSK3β, suppresses tau phosphorylation, and reduces amyloid-beta production—key pathological features of AD (11,21).

Strikingly, CASE #1 presented an episode of delirium during follow-up, which was evident in cognitive performance and showed cognitive recovery, contrasting with studies linking delirium to long-term decline (22). In this regard, the literature describes a role for circulating Reelin in proinflammatory phenomena.

Circulating Reelin is predominantly synthesized by hepatic stellate cells, which remain quiescent until activated by liver injury, subsequently contributing to the production of the collagen-rich extracellular matrix characteristic of hepatic fibrosis (23). Notably, circulating Reelin can also activate ApoER2 on vascular endothelial cells, inducing the expression of NF-κB–dependent adhesion molecules—a mechanism that may link systemic aging and inflammation to central nervous system pathology (24–26). This peripheral proinflammatory role contrasts with the neuroprotective function of Reelin within neuronal circuits, suggesting that its net physiological impact is governed by the dynamic interplay between neuroprotective and proinflammatory signaling cascades (27).

Although the peripheral behavior of *REELIN*-COLBOS has not been described, the gain-of-function in relation to the canonical signaling pathway initially described would suggest that a greater balance in inflammatory mechanisms can be maintained even at an advanced age.

In the other cases (#2 to #5), we noted a high burden of comorbidities. Also, the fact that all five *REELIN*-COLBOS carriers identified were women aligns with the female predominance among centenarians (28).

Previous studies from our laboratory have revealed a sex-specific dimorphism, whereby male *REELIN*-COLBOS mice exhibited a more pronounced protective phenotype, including elevated levels of phosphorylated Dab1 and more marked tau-related outcomes (17). However, the predominance of women in our oldest old cohort may account for other protective factors that are not exclusively genetic, such as cultural, historical, and environmental factors (28).

Another important convergence pathway that could be related to the role of *REELIN*-COLBOS in longevity is the insulin/IGF-1 signaling pathways.

Although a direct link has not been established, the Reelin and insulin/IGF-1 signaling pathways share common downstream components, including overlap in the Akt pathway, which inhibits GSK3β and FoxO transcription factors and modulates mTORC1 activity (9,29). Given that multiple longevity-promoting interventions have targeted insulin/IGF-1 signaling, this convergence suggests that combined modulation of Reelin signaling may offer additive cognitive benefits in the context of aging. Moreover, both genetic and pharmacological reduction of circulating Reelin levels has been shown to exert a protective effect against atherosclerosis (30).

While limited by short follow-up and targeted genetic analysis, these cases highlight the need for further research on sex-specific effects of *REELIN*-COLBOS in cognitive aging.

This study has some limitations, including the short duration of follow-up, which limits our ability to evaluate additional environmental factors that may contribute to resilience. The sample size is also small and not representative of the Colombian population at large. Moreover, only a narrow set of genetic variants was assessed, so the influence of other protective factors cannot be excluded.

Despite these limitations, we describe five aging well cases among *REELIN*-COLBOS carriers. This corresponds to an unusually high prevalence of this variant for a sample collected by snowball sampling. Additionally, a review of the literature on mechanisms and pathways related to Reelin would support a possible protective role for REELIN-COLBOS in aging.

Further studies are needed to elucidate these mechanisms and explore *REELIN*-COLBOS in other systems, such as its role in the circulatory system and as an inflammatory mediator, in order to better understand the protective effects of this variant.

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Competing interests

JFA, YTQ and FL are co-inventors on a pending patent that leverages Reelin therapeutics. JFA is a co-founder of Epoch Biotech, a company developing Reelin-COLBOS-inspired therapeutics. YTQ serves as a consultant for Biogen.

Data availability statement

The data that support the findings of this study are available upon reasonable request. Requests for access to the data should be directed to the corresponding authors Yakeel T. Quiroz, Ph.D. yquiroz@bu.edu and Joseph F. Arboleda-Velasquez, M.D., Ph.D joseph_arboleda@meei.harvard.edu.

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Supplementary data

Supplementary Table 1. Allelic frequency of the variants highlighted in the oldest olds (N = 135).

Protein [SNP ID]	**Allele frequency in the admixed American population from gnomAD browser***	**Allelic frequency in the oldest old, n (%)**
REELIN-COLBOS [Ch7:103113302 T>C]	0.00005784	5 (1.9%)**
***PSEN1*-E280A** [Chr14:73664808 A>C]	0	0 (0%)
APOE2 [rs7412 Chr19:44908822 C>T]	0.03489	23 (8.5%)
APOE4 [rs429358 chr19:44908684 T>C]	0.1069	31 (11.5%)***
APOECh [rs121918393 chr19:44908756 C>A]	0.0001536	0 (0%)

SNP ID = Single Nucleotide Polymorphism identification code

* https://gnomad.broadinstitute.org/

** Two *REELIN-COLBOS* carriers were also *APOE* ε2, and *APOE* ε4 carriers, respectively.

*** Two were homozygous for *APOE* ε4.

Supplementary Table 2. Clinical scales of each follow-up.

Test	Index case (Case #1)			Case #2		Case #3				Case #4			Case #5
	102 yr.	102 yr. + 7 mo.	104 yr.	82 yr.	85 yr.	91 yr.	94 yr.	96 yr.	98 yr.	74 yr.	82 yr.	93 yr.	90 yr.
	Score	Score	Score	Score	Score	Score	Score	Score	Score	Score	Score	Score	Score
Geriatric Depression Scale (Yesavage)	1	0	5	2	2	0	0	3	0	3	0	2	3
GAD-7	NA	2	1	NA	1	NA	0	8	0	NA	NA	0	11
Complaints Scales (Caregiver - Patient)	NA - 14	32 - 27	jun-28	13 - 27	7-ago	8-jun	21 - 26	25 - 21	41 - 31	mar - 22	NA - 14	22-jun	20 - 21
FAST	4	6	4	2	1	1	4	5	6	2	1	4	3

FAST = Functional Assessment Staging scale; GAD-7 = Generalized Anxiety Scale - 7; NA = not apply/missing.

Supplementary Table 3. Neuropsychological follow-up of cases 2 and 3.

Domain	Test	Case #2		Case #3			
		82 yr.	85 yr.	91 yr.	94 yr.	96 yr.	98 yr.
		Score (Z)	Score (Z)	Score (Z)	Score (Z)	Score (Z)	Score (Z)
Global	MMSE /30	29 (1.7)	22 (-1.3)	30 (2.2)	20 (-2.2)	16 (-3.9)	12 (-5.6)
Language	Semantic Fluency - Animals	19 (1.6)	11 (-0.3)	12 (-0.1)	5 (-176)	6 (-1.4)	5 (-1.6)
Memory (verbal)	CERAD Word List Learning Total Score /30	13 (0.2)	13 (0.2)	11 (-0.4)	12 (-0.1)	8 (-1.2)	6 (-1.8)
	CERAD Word List Learning Recall /10	4 (0.7)	6 (1.9)	2 (-0.5)	0 (-1.8)	0 (-1.7)	0 (-1.7)
	CERAD Word List Learning Recognition /10	10 (1.1)	8 (0.1)	2 (-3.1)	3 (-2.6)	0 (-4.2)	1 (-3.6)
Memory (visual)	CERAD Constructional Praxis Recall /11	2 (-0.5)	0 (-1.2)	1 (-0.9)	0 (-1.2)	0 (-1.2)	NA (.)
Perceptual-motor	CERAD Constructional Praxis Copy /11	8 (0.8)	6 (-0.2)	7 (0.3)	5 (-0.7)	2 (-2.2)	NA (.)
Executive	Phonemic Fluency- F-A-S	21 (-0.3)	13 (-1.1)	17 (-0.7)	11 (-1.5)	3 (-2.2)	NA (.)

CERAD = Consortium to Establish a Registry for Alzheimer's Disease; MMSE = Mini-Mental State Examination; NA = not apply/missing; Z = Z-score.

Supplementary Table 4. Neuropsychological follow-up of cases 4 and 5.

Domain	Test	Case #4			Case #5
		74 yr.	82 yr.	93 yr.	90 yr.
		Score (Z)	Score (Z)	Score (Z)	Score (Z)
Global	MMSE /30	29 (1.7)	28 (1.3)	16 (-3.9)	19 (-2.6)
Language	Semantic Fluency-Animals	11 (-0.3)	11 (-0.3)	3 (-2.2)	9 (-0.8)
Memory (verbal)	CERAD Word List Learning Total Score /30	16 (1.1)	12 (-0.1)	6 (-1.9)	18 (1.7)
	CERAD Word List Learning Recall /10	6 (1.9)	3 (0.1)	0 (-1.8)	3 (0.1)
	CERAD Word List Learning Recognition /10	10 (1.1)	10 (1.1)	1 (-3.7)	10 (1.1)
Memory (visual)	CERAD Constructional Praxis Recall /11	2 (-0.5)	4 (0.2)	0 (-1.2)	0 (-1.2)
Perceptual-motor	CERAD Constructional Praxis Copy /11	9 (1.2)	10 (1.7)	5 (-0.7)	6 (-0.2)
Executive	Phonemic Fluency-F-A-S	NA (.)	NA (.)	8 (-1.5)	26 (0.1)

CERAD = Consortium to Establish a Registry for Alzheimer's Disease; MMSE = Mini-Mental State Examination; NA = not apply/missing; Z = Z-score.