Table A1: Summary of Studies of Cognition in the Colombian Kindred

Authors	Year	Key findings in *PSEN1* E280A carriers
Lopera et al.	1997	The clinical manifestation of *PSEN1* E280A was similar to that of sporadic AD, although carriers with dementia frequently complained of headaches
Ardilla et al. Arango-Lasprilla et al. Aguirre-Acevedo et al	2000 2007 2016	Short-term verbal memory deficits were seen in carriers in the decade prior to MCI; attention and concentration problems were also common
Rosselli et al.	2000	Mutation carriers with dementia performed worse than age-matched non-carriers at baseline on all neurocognitive measures except word reading; these carriers showed decline over an 18-month period across all neurocognitive tests, with the greatest decline occurring on the Mini Mental State Exam
Lasprilla et al.	2003	Mutation carriers with AD performed worse on 29 of 43 neuropsychological tests relative to carriers without cognitive symptoms
Tirado et al.	2004	*PSEN1* E280A mutation carriers had more intrusions on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) verbal memory test, and more semantic errors on the CERAD naming test relative to non-carrier family members
Cuentos et al.	2007	*PSEN1* E280A mutation carriers produced fewer semantic categories when describing a visual scene than non-carrier family members
Parra et al.	2010 2011 2015	Visual short-term memory issues differentiated *PSEN1* E280A carriers from non-carriers; shape-color binding difficulties related to white-matter integrity in clinically demented *PSEN1* E280A carriers
Acosta-Baena et al.	2011	Clinical characterization of *PSEN1* E280A; demented carriers presented with memory loss, anomia, personality changes, and headaches.
Norton et al.	2017	Informant-based report of subjective cognitive decline corresponded with hippocampal volume in *PSEN1* E280A carriers

Table A2: Studies of Brain Function in *PSEN1* E280A ADAD

Imaging modality	Authors	Year	Key findings in *PSEN1* E280A carriers
Electroencephalogram	Bobes et al.	2010	Increased N400 signal seen in left temporal areas in preclinical carriers; cognitively impaired carriers had decreased N400 signal in right temporal and cingulate areas
	Quiroz et al.	2011	Decreased frontal positivity and increased occipital positivity
	Duque-Grajales et al.	2014	Greater theta synchronization seen when comparing task activity to rest
	Rodriguez et al.	2014	Beta-band frequency alternation in the frontal lobe during memory task encoding
	Suárez-Revelo et al.	2016	Right-occipital lobe showed less output strength in carriers with MCI or AD relative to preclinical carriers and non-carriers
	Ochoa et al.	2017	Default mode network hyperactivity
	Penny et al.	2018	Greater activation in medial temporal lobe (MTL) of carriers during a semantic picture matching task; cognition predicted by strength of connections within MTL
Functional Magnetic Resonance Imaging	Quiroz et al.	2010	Preclinical carriers exhibited greater activation in the right cingulate gyrus and right anterior hippocampus during face-name encoding
	Reiman et al.	2012	Carriers showed greater activation during encoding in the right hippocampus and parahippocampal gyrus, as well as less deactivation in the precuneus and posterior cingulate cortex
	Quiroz et al.	2015	Child carriers exhibited less encoding-related deactivation of parietal regions and greater connectivity in the default mode network relative to non-carriers
	Quiroz et al.	2015	Preclinical carriers showed greater activation of the hippocampus and parahippocampal gyri during scene encoding
Fludeoxyglucose Positron Emission Tomography	Fleisher et al.	2013	Preclinical and demented carriers had decreased glucose metabolism in temporal and parietal regions, seen as early as 18 years before the onset of MCI
Single-Photon Emission Computed Tomography	Johnson et al.	2001	Decreased cerebral profusion in hippocampal, frontal, parietal, and cingulate areas

Table A3: Studies of Brain Structure in *PSEN1* E280A ADAD

Imaging modality	Authors	Year	Key findings in *PSEN1* E280A carriers
Structural Magnetic Resonance Imaging (MRI)	Lopera et al.	1999	Perihippocampal fissures common in symptomatic carriers and differentiated carriers from non-carriers; distance between the unci of the temporal lobe also distinguished symptomatic carriers from non-carriers
	Quiroz et al.	2012	Cortical thickness in child and young adult carriers did not differ relative to non-carriers; older adult carriers (EYO of ~6 years) show significant thinning in all AD-signature regions
	Reiman et al.	2012	Young adult mutation carriers show thinning of grey matter in the right parietal lobe relative to non-carriers
	Quiroz et al.	2013	Cortical thinning seen in AD-signature regions of the parietal and temporal lobes
	Quiroz et al.	2015	Child carriers do not show grey matter volume neurodegeneration relative to non-carriers
Diffusion tensor imaging	Parra et al.	2015	White matter was degenerated in demented carriers, most saliently in the mid-frontal lobe and genu of the corpus callosum

Table A4: Studies of Alzheimer's disease pathology in *PSEN1* E280A ADAD

Biomarker Modality	Authors	Year	Key findings in *PSEN1* E280A carriers
Cerebral Spinal Fluid (CSF) and Plasma Markers of Alzheimer's disease Pathology	Reiman et al.	2012	Elevated plasma $A\beta_{1-42}$ and cerebral spinal fluid (CSF) $A\beta_{1-42}$ distinguished young adult mutation carriers from non-carriers
	Quiroz et al.	2015	Child mutation carriers showed elevated plasma Aβ1-42 and elevated Aβ1-42: Aβ1-40 ratios
Amyloid PET	Fleisher et al.	2012	Cortical Aβ aggregation was evident in carriers with an EYO of -16 years, rising steeply until plateauing at -6 EYO; accumulation of Aβ was most apparent in regions of the parietal and frontal lobes, as well as the basal-ganglia
	Quiroz et al.	2018	Cortical Aβ aggregation seen at an EYO of -15 years
Tau PET	Quiroz et al.	2018	Tau deposition apparent in carriers beginning at an EYO of -6 years in regions of the temporal lobe; wide-spread aggregation of tau throughout the brain is seen as carriers progress to MCI; tau is more strongly associated with cognitive performance than cortical Aβ in carriers
Alzheimer's disease biomarker trajectory modeling	Quiroz et al.	2015	Cortical Aβ and CSF phosphorylated-tau/Aβ1-42 ratios predict cognitive decline in carriers near symptom onset
	Fleisher et al.	2015	Biomarker abnormalities in carriers were estimated to occur in the following sequence, beginning more than 2 decades before the onset of MCI: CSF Aβ1-42, cortical Aβ, precuneus glucose metabolism, CSF total tau, temporal lobe tau, hippocampal volume