

Framingham Neuropsychological Test Database

One of the key strengths of Framingham's Cognitive Aging studies is the extensive existing database that includes incident surveillance for dementia/Alzheimer's disease, stroke and Parkinson's disease, consistent application of diagnostic criteria for disease diagnosis, longitudinal measures of cardiovascular and metabolic risk factors, as well as lifestyle and functional behaviors, a wide range of plasma biomarkers, multiple NP assessments and brain MRI scans, and genetic risk factors for AD/dementia. The data highlighted below are those of specific interest to AD research, but does not fully represent all available FHS data.

Biomarkers and risk factors associated with cognition and dementia/AD.

Additionally, in 2008, the National Heart, Lung and Blood Institute (NHLBI) of the National Institute of Health (NIH) measured 150+ novel serum/plasma/urine biomarkers of

<i>Demographic data</i>	Age, sex, education, occupation, socio-economic status, current residence
<i>Lifestyle Factors</i>	
Diet	Willett Food Questionnaire, fish, coffee, tea, soda, supplements
Legal substance use	Smoking, Alcohol
Physical & leisure activities	Physical activity index, physical fitness on exercise testing, physical activity questionnaire
Sleep	polysomnographic measures; sleep duration/quality questionnaire
Functional Measures	Katz Activities of Daily Living, Rosow Breslau & Nagi scales; Guralnik Short Physical Performance Battery
Depression, social network	Center for Epidemiologic Studies scale for Depression (CES-D) scores, SF-12 and Berkman-Syme social network index
<i>Vascular/Metabolic Risk Factors</i>	
Cardiovascular Risk Factors	Systolic, diastolic and pulse pressures; hypertension, diabetes, atrial fibrillation and plasma cholesterol
Vascular injury	Carotid stenosis and intima-media thickness; brachial reactivity/endothelial function; tonometric arterial stiffness, echocardiographic left ventricular mass, and cardiac-output; CT coronary calcium burden; cardiac structure and aortic arch plaques on cardiac MRI; ankle brachial index; pulse wave velocity
Anthropometric/adiposity indices	Height, weight, body-mass index, waist circumference, waist-hip ratio, sagittal abdominal diameter, CT measurements of subcutaneous and visceral fat
<i>Plasma Biomarkers</i>	
APOE	ε2,ε3 and ε4 genotype and circulating APOEε4 levels
Amyloid burden	Plasma Aβ40 and Aβ42
Polyunsaturated fatty-acids	Docasohexaenoic acid (DHA), Total Omega-3 fatty-acids, other RBC membrane fatty-acid
Inflammation	C-reactive protein (CRP), interleukin 6 (IL-6), intercellular adhesion molecule (ICAM1), myeloperoxidase, osteoprotegerin, P-selectin, CD40 ligand, monocyte chemoattractant protein-1, intercellular adhesion molecule-1 (ICAM-1), TNF-alpha and its receptor TNF-R2, and lp-PLA2
Hemostatis, Thrombosis	Fibrinogen, Factor VIIIc, von Willebrand factor, D-dimer, PAI-1
Lipid Metabolism	Total cholesterol, Low- & high-density lipoprotein cholesterol (LDL-C, HDL-C), apolipoprotein (apo) A-I & B, lipid ratios (total cholesterol:HDL-C, LDL-C:HDL-C, apo B:apo A-I), lipoprotein (a).
Molecules interacting with Vessel Wall and Platelets	Markers of matrix remodeling (MMP-9, MMP-3, TIMP-1, PIINP, Plasma homocysteine, Asymmetric dimethylarginine (ADMA)
Oxidative Stress	Isoprostanes, uric acid
Hormones	Renin-angiotensin-aldosterone pathway, measures of thyroid function (such as TSH), sex steroid hormones, natriuretic pathway peptides (such as BNP, NT-ANP)
Vitamins	Folate, unmetabolized folate, B ₁₂ , B ₆ , Vitamin D
Growth Factors and receptors	IGF-1, VEGF, BDNF, NGF, SORL1, SORT1, TRKA, TRKB
Adipokines	Leptin, resistin, tumor necrosis factor alpha (TNF) and receptor (TNFR2), adiponectin.
Glycemic control and insulin resistance	HbA1C, Fasting and Postprandial blood sugar, categorization as impaired fasting glucose (IFG), impaired glucose tolerance (GT), fasting and post-prandial insulin levels, measures of insulin resistance: HOMA-IR and Insulin Sensitivity Index (ISI)
Brain Injury	S-100b (an astroglial protein), NSE (neuron-specific enolase, a marker of neuronal injury), GFAP (glial fibrillary acidic protein, marker of glial injury)
<i>Clinical Events/Co-Morbidities</i>	stroke, Parkinson's disease, seizures, myocardial infarction, congestive heart failure, cancer, osteoporosis, chronic obstructive pulmonary disease

NP Tests: The set of all FHS subjects that have had a NP evaluation, beginning in 1/3/1982 to 1/31/2020.

Table 3: Number of Participants with NP Exams			
	1+	2+	3+
NP evaluation	7526	4798	2487
Generation 1	1411	839	527
Generation 2	3073	2332	1698
Generation 3	2511	1331	129
OmniGen 1	337	216	129
OmniGen 2	150	68	2
New Offspring Spouses	44	12	2
*as of 01/31/20			

Kaplan-Albert NP Tests: The set of all FHS subjects that have had a NP evaluation with the Kaplan-Albert battery, which was in use from 1976 to 1968.

Table 4: Number of Participants with Kaplan-Albert NP Exams			
	1+	2+	3+
Generation 1	2123	0	0
*as of 1/31/20			

Digital voice/pen data: To further enhance the sensitivity of NP testing for detecting impairment, since 2005 FHS has digital voice data for spoken responses and since 2011 used a digital pen in place of a regular ballpoint pen for participant drawn tests. The digital technologies allow collection of decision-making latencies and other behavioral characteristics that may reflect underlying cognitive processing that traditional pen and pencil tests cannot measure.

Table 5: Number of Participants with Digital Voice/Pen Data			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	5411	3002	863
Digital Pen (Clock)	3653	1082	67
Digital Pen (NP)	3000	667	48
*as of 01/31/20			

Table 6: Generation 1			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	201	96	49
Digital Pen (Clock)	10	2	1
Digital Pen (NP)	10	2	0
*as of 01/31/20			

Table 7: Generation 2			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	2301	1502	720
Digital Pen (Clock)	1563	721	53
Digital Pen (NP)	1387	483	40
*as of 01/31/20			

Table 8: Generation 3			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	2483	1242	73
Digital Pen (Clock)	1727	269	11
Digital Pen (NP)	1288	128	7
*as of 01/31/20			

Table 9: OmniGen 1			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	244	118	18
Digital Pen (Clock)	183	32	1
Digital Pen (NP)	174	31	1
*as of 01/31/20			

Table 10: OmniGen 2			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	142	33	1
Digital Pen (Clock)	131	49	1
Digital Pen (NP)	110	20	0
*as of 01/31/20			

Table 11: New Offspring Spouses			
	# of tests (n=# of unique participants*		
	1+	2+	3+
Digital Voice	40	11	2
Digital Pen (Clock)	39	9	0
Digital Pen (NP)	31	3	0
*as of 01//31/20			

Brain MRI scans. A subset of FHS subjects also had an MRI scan concurrent with each NP evaluation, beginning in 1999

Table 12: Number of Participants with Brain MRI scans			
	+1	2+	3+
MRI scans	5538	2968	1258
Generation 1	280	155	102
Generation 2	2539	1752	1061
Generation 3	2266	867	3
OmniGen 1	296	173	92
OmniGen 2	131	12	0
New Offspring Spouses	26	0	0
*as of 01/31/20			