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## The elusive nature of APOE e4 in mid-adulthood: understanding the cognitive profile

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### APOE: the cognitive profile in mid-adulthood

First Author (year)	n	Age: mean (range)	Gender (% M)	Ethnicity	Cognitive domains	Neuropsychological tasks	Zygosity
Bender (2012)	72	50 (19-77)	-	74% Caucasion, 26% other.	G, EM, EA, PS	MMSE, Word recognition task (individual, paired association), Size judgement span, Spatial recall, Listening span, n-back; Letter same-different (PS), Pattern same-different (PS)	ε4- vs. ε4+ (ε3/ε3, vs. ε3/ε4, ε4/ε4)
		56	51	6202 Caucasian	EM EA		<b>1.</b> ε2+ vs. ε3 vs. ε4 He vs. ε4 Ho
Blair (2005)	6810	(45-64)	38	1693 African- American	VF DWR, DSS, VF		(ε2/ε2; ε2/ε3 vs. ε3/ε3 vs. ε2/ε4, ε3/ε4 vs. ε4/ε4) <b>2.</b> ε4- vs. ε4+
Caselli (1999)	100	56 (49-69)	28	-	EM, EA, VF, L, VS	AVLT, WAIS DS, WAIS Mental arithmetic, COWAT, WAIS Similarities, BNT, CFT, WAIS Block design	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 3/ $\epsilon$ 3, vs. $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Caselli (2011)	621	59 (21+)	30	-	EM, EA, VF, PS	AVLT, COWAT, DSS, PASAT, WCST	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 3/ $\epsilon$ 3, vs. $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Chen (2013)	18	42 (-)	44	-	G, EA	MMSE, <i>n</i> -back	ε4- vs. ε4 He (ε2/ε2, ε2/ε3, ε3/ε3 vs. ε3/ε4)
Deeny (2008)	54	60 (50-70)	56	-	EA	Sternberg WM task	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3, vs. $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Donix (2010)	28	55.3 (38-63)	~23	-	G, EM, EA,VF, L, VS	MMSE, WMS (logical memory-delayed, verbal paired associates), Buschke selective reminding test, DS (forward, backward), Stroop interference, WCST, TMT-B, VF, BNT, CFT	ε4- vs. ε4+ (ε2/ε3, ε3/ε3, vs. ε3/ε4, ε4/ε4)

Table 1. Overview of cross-sectional studies investigating APOE genotype differences in mid-adulthood.

Flory (2000)	220	47 (24-60)	51	-	EM, EA	Verbal learning, Verbal delayed recall, Figure delayed recall, DS (forward, backward), Recurring word test	$\begin{array}{c} \epsilon 4\text{- vs. } \epsilon 4\text{+ } (\epsilon 2/\epsilon 2,  \epsilon 2/\epsilon 3,  \epsilon 3/\epsilon 3,  \text{vs.} \\ \epsilon 2/\epsilon 4,  \epsilon 3/\epsilon 4,  \epsilon 4/\epsilon 4) \end{array}$
Goveas (2013)	46	54 (44-65)	33	-	EM, EA, PS	AVLT, TMT-A & B, DS	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3, vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Greenwood (2000)	97	59 (50+)	39	-	EM, EA	WMS General, WMS Delayed, Buschke selective reminding test, Cued letter discrimination task, Vigilance task, Dynamic scaling	ε2+ vs. ε3 vs. ε4+ (ε2/ε2; ε2/ε3 vs. ε3/ε3 vs. ε2/ε4, ε3/ε4, ε4/ε4)
Greenwood (2005a)	177	59 (41-85)	41	-	EA	Cued letter discrimination task, Spatial WM task, Attention/WM task	ε4- vs. ε4 He vs. ε4 Ho (ε2/ε2, ε2/ε3, ε3/ε3 vs. ε2/ε4, ε3/ε4 vs. ε4/ε4
Greenwood (2014)	591	50 (40-59)	-	92% Caucasian	EA	MMSE, WAIS logical memory, WAIS letter- number sequencing, Delayed match-sample task	$\begin{array}{c} \epsilon 4\text{-} \text{ vs. } \epsilon 4\text{+} (\epsilon 2/\epsilon 2, \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3, \text{ vs.} \\ \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4, \epsilon 4/\epsilon 4)\end{array}$
Jorm (2007)	2176	- (40-44)	47	-	EM, EA, L, PS	CVLT, DS (backward), Spot-the-word, DSS	ε4- vs. ε4 He vs. ε4 Ho (ε2/ε2, ε2/ε3, ε3/ε3 vs. ε2/ε4, ε3/ε4 vs. ε4/ε4
Langbaum (2010)	27	55 (47-68)	19	Latino	G, EM, EA, VF, L, VS	MMSE, WAIS, AVLT, COWAT, BNT, CFT	ε4- vs. ε4+ (ε2/ε3, ε3/ε3, vs. ε2/ε4, ε3/ε4, ε4/ε4)
Levy (2004)	176	59 (42-86)	36	-	EM, VF, VS, L, PS	WMS Logical Memory I & II, Buschke Selective Reminding Test, WMS Verbal Paired Associations I & II, WMS Visual Reproduction I & II, Verbal fluency (letter, category), BNT, CFT, Block design, DSS	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3, vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Marioni (2016)	12 472	42 (19-59)	41	-	EM, VF, L, PS	WAIS Logical memory, VF, Mill Hill Vocabulary scale, DSS	$\epsilon 2/\epsilon 2$ vs. $\epsilon 2/\epsilon 3$ vs. $\epsilon 2/\epsilon 4$ vs. $\epsilon 3/\epsilon 3$ vs. $\epsilon 3/\epsilon 4$ vs. $\epsilon 4/\epsilon 4$
Nichols (2012)	133	36 (19-77)	44	Caucasian	G, EM	WAIS, Recognition memory task	ε2/ε3 vs. ε3/ε3 vs. ε3/ε4
Oberlin (2015)	975	45 (30-54)	49	Caucasian	EM, EA	WMS Logical memory, WMS Visual reproduction, TMT-A & B	$\begin{array}{c} \epsilon 4\text{-} \text{ vs. } \epsilon 4\text{+} (\epsilon 2/\epsilon 2, \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3, \text{ vs.} \\ \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4, \epsilon 4/\epsilon 4) \end{array}$
Panizzon (2014)	717	56 (51-60)	100	89.7% Caucasian	EM	CVLT, WMS Story recall, WMS Figure recall	ε4- vs. ε4+ (ε2/ε2, ε2/ε3, ε3/ε3, vs. ε2/ε4, ε3/ε4, ε4/ε4)

Patel (2013)	36	45 (-)	42	72% Caucasian, 19% Afro- American, 9% Other	G, EM, EA, VF, PS	IQ, WRAT, BVMT (delayed recall, recognition), DS, VF, Groove-pegboard task, Letter-number sequencing, Symbol search, TMT A & B	ε4- vs. ε4+ (ε2/ε3, ε3/ε3, vs. ε3/ε4, ε4/ε4)
Protas (2013)	149	56 (47-68)	36	-	G, EM, VF, VS, L	MMSE, WAIS, AVLT, CFT, COWAT, BNT	$\epsilon$ 4- vs. $\epsilon$ 4 He vs. $\epsilon$ 4 Ho ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4 vs. $\epsilon$ 4/ $\epsilon$ 4
Ready (2011)	23	56 (46-66)	39	-	EM, EA, VF	Memory composite (WMS Logical, CVLT, WMS Visual Reproduction), Trail-making composite, Colour-word composite, VF composite (letter, category)	ε4- vs. ε4+ (ε2/ε3, ε3/ε3 vs. ε3/ε4)
Sager (2005)	452	53 (40-65)	29	-	EM, EA, VF, L, VS	AVLT, Faces I and II, Stroop-colour, TMT-B, WCST, WAIS WM index, VF, WAIS Vocabulary, Similarities, Word-reading, BNT, WAIS Block design, Matrix reasoning, Line orientation judgment	ε4- vs. ε4+ (ε2/ε2, ε2/ε3, ε3/ε3, vs. ε2/ε4, ε3/ε4, ε4/ε4)
Schultz	626	55 (50-59)	100	-	EM	WMS Logical Memory, WMS Visual Reproduction	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
(2008)		(50-57)				1	
(2008)	2401	(50-57) 45-54	36	-			$\epsilon$ 4- vs. $\epsilon$ 4 He vs. $\epsilon$ 4 Ho ( $\epsilon$ 2/ $\epsilon$ 2,
(2008) Shin (2014)	2401 3919	(50-57) 45-54 55-64	36 39	-	G	Korean MMSE	$\epsilon$ 4- vs. $\epsilon$ 4 He vs. $\epsilon$ 4 Ho ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4 vs. $\epsilon$ 4/ $\epsilon$ 4)
(2003) Shin (2014) Sunderland (2004)	2401 3919 142	(50-57) 45-54 55-64 59 (-)	36 39 37	- -	G G	Korean MMSE MMSE, BNT	$\epsilon$ 4- vs. $\epsilon$ 4 He vs. $\epsilon$ 4 Ho ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4 vs. $\epsilon$ 4/ $\epsilon$ 4) $\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Shin (2014) Sunderland (2004) Trachtenberg (2012)	2401 3919 142 72	(30-57) 45-54 55-64 59 (-) 46 (30-55)	36 39 37 48	- - -	G G EM, EA	Korean MMSE MMSE, BNT Episodic retrieval-pictures; Counting Stroop task	$\begin{array}{c} \epsilon 4- \text{ vs. } \epsilon 4 \text{ He vs. } \epsilon 4 \text{ Ho } (\epsilon 2/\epsilon 2, \\ \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4 \text{ vs.} \\ \epsilon 4/\epsilon 4) \\ \epsilon 4- \text{ vs. } \epsilon 4+ (\epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 2/\epsilon 4, \\ \epsilon 3/\epsilon 4, \epsilon 4/\epsilon 4) \\ \epsilon 2 \text{ vs. } \epsilon 3. \ \epsilon 4 \text{ He vs. } \epsilon 4\text{Ho } (\epsilon 2/\epsilon 3 \text{ vs.} \\ \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 3/\epsilon 4 \text{ vs. } \epsilon 4/\epsilon 4) \end{array}$
(2003) Shin (2014) Sunderland (2004) Trachtenberg (2012) Velichkovsky (2015)	2401 3919 142 72 35	(30-59) 45-54 55-64 59 (-) 46 (30-55) 50 (-)	36 39 37 48 26		G G EM, EA EM, EA	Korean MMSE MMSE, BNT Episodic retrieval-pictures; Counting Stroop task AVLT, WMS Visual reproduction, Anti- saccade task, Switching task, <i>n</i> -back task, Operation span	$\begin{array}{c} \epsilon 4- \text{ vs. } \epsilon 4 \text{ He vs. } \epsilon 4 \text{ Ho } (\epsilon 2/\epsilon 2, \\ \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4 \text{ vs.} \\ \epsilon 4/\epsilon 4) \\ \epsilon 4- \text{ vs. } \epsilon 4+ (\epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 2/\epsilon 4, \\ \epsilon 3/\epsilon 4, \epsilon 4/\epsilon 4) \\ \epsilon 2 \text{ vs. } \epsilon 3. \epsilon 4 \text{ He vs. } \epsilon 4\text{Ho } (\epsilon 2/\epsilon 3 \text{ vs.} \\ \epsilon 3/\epsilon 3 \text{ vs. } \epsilon 3/\epsilon 4 \text{ vs. } \epsilon 4/\epsilon 4) \\ \epsilon 3 \text{ Ho vs. } \epsilon 4 \text{ Hz } (\epsilon 3/\epsilon 3 \text{ vs. } \epsilon 3/\epsilon 4) \\ \end{array}$
Shin (2014) Sunderland (2004) Trachtenberg (2012) Velichkovsky (2015)	2401 3919 142 72 35 74	(30-59) 45-54 55-64 59 (-) 46 (30-55) 50 (-) 59 (50-65)	36 39 37 48 26 27	- - - -	G G EM, EA EM, EA EM	Korean MMSE MMSE, BNT Episodic retrieval-pictures; Counting Stroop task AVLT, WMS Visual reproduction, Anti- saccade task, Switching task, <i>n</i> -back task, Operation span Recognition memory task	$\epsilon 4- vs. \epsilon 4 He vs. \epsilon 4 Ho (\epsilon 2/\epsilon 2, \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 vs. \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4 vs. \epsilon 4/\epsilon 4)$ $\epsilon 4- vs. \epsilon 4+ (\epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3 vs. \epsilon 2/\epsilon 4, \epsilon 3/\epsilon 4, \epsilon 4/\epsilon 4)$ $\epsilon 2 vs. \epsilon 3. \epsilon 4 He vs. \epsilon 4 Ho (\epsilon 2/\epsilon 3 vs. \epsilon 3/\epsilon 3 vs. \epsilon 3/\epsilon 4 vs. \epsilon 4/\epsilon 4)$ $\epsilon 3 Ho vs. \epsilon 4 Hz (\epsilon 3/\epsilon 3 vs. \epsilon 3/\epsilon 4)$ $\epsilon 4- vs. \epsilon 4+ (\epsilon 2/\epsilon 2, \epsilon 2/\epsilon 3, \epsilon 3/\epsilon 3, vs. vs. vs. vs. vs. vs. vs. vs. vs. vs.$

Abbreviations: Domains: Global (G), Memory (M), Executive abilities (EA), Verbal Fluency (VF), Language (L), Visuospatial processing (VS), Processing Speed (PS). Tasks: Mini-mental State Examination (MMSE), Wide Range Achievement Test (WRAT), Delayed Word Recall (DWR), Brief Visuospatial Memory test (BVMT), Rey's Auditory verbal learning task (AVLT), Californian verbal learning test (CVLT), Digit span (DS), Paced Auditory Serial Attention task (PASAT), Prospective memory (PM), Rapid Visual Information Processing task (RVIP), Trails-making test (TMT), Wisconsin Card Sort task (WCST), Complex figure test (CFT), Controlled oral association task (COWAT), Boston Naming Task (BNT), Digit-symbol Substitution (DSS). Zygosity: Heterozyous (He), Homozygous (Ho)

Domain	Authons (year)	Group n					
Domani	Authors (year)	Age (M)	ε4+	ε4-	Hedge's d		
Global	Bender (2012)	50	20	52	0.45		
	Donix (2010)	55	12	16	-0.02		
	Langbaum (2010)	55	11	16	0.00		
	Nichols (2012)	36	35	81	-0.21		
	Patel (2013)	45	14	22	0.21		
	Protas (2013)	56	73	76	0.00		
	Shin (2014) (45-54)	-	380	1967	0.09		
	Shin (2014) (55-64)	-	679	3240	-0.12		
	Sunderland (2004)	59	57	85	0.22		
Memory	Blair (2005) (C)	56	1720	3648	0.00		
	Blair (2005) (A)	56	698	744	0.00		
	Caselli (2011)	59	265	356	-0.03		
	Caselli (1999)	56	50	50	-0.13		
	Donix (2010)	59	12	16	0.03		
	Evans (2013; 2014)	50	19	21	-0.45		

Table 2. Average effect size per study organised by cognitive domain, where a positive effect size represents better performance by the  $\varepsilon 4$ + group

Flory (2000)	47	61	159	-0.27
Greenwood (2000)	59	38	48	-0.26
Goveas (2013)	54	20	26	-0.48
Jorm (2007)	-	611	1571	0.01
Langbaum (2010)	55	11	16	0.08
Levy (2004)	59	61	115	-1.94
Marioni (2016)	42	3807	8665	-0.01
Nichols (2012)	36	35	81	-0.18
Patel (2013)	45	14	22	-0.28
Protas (2013)	56	73	76	0.09
Sager (2005)	53	204	248	0.05
Trachtenberg (2012)	46	33	20	-0.16
Velichkovsky (2015)	50	13	22	-0.23
Xu (2009)	58	18	25	0.35
Caselli (1999)	56	50	50	0.06
Caselli (2011)	59	265	356	0.05
Chen (2013)	42	9	9	0.20
Donix (2010)	59	12	16	-0.01
Evans (2013; 2014)	50	19	21	0.36
Flory (2000)	47	61	159	-0.09
Goveas (2013)	54	20	26	-0.54
Jorm (2010)	-	611	1571	-0.06
Langbaum (2010)	55	11	16	0.26
Sager (2005)	53	204	248	-0.06
Trachtenberg (2012)	46	33	20	-0.17
Velichkovsky (2015)	50	13	22	-0.15

Executive abilities

Verbal Fluency	Blair (2005) (C)	56	1720	3648	0.00
	Blair (2005) (A)	56	698	744	-0.06
	Caselli (2011)	59	265	356	0.01
	Donix (2010)	55	12	16	-0.02
	Langbaum (2010)	55	11	16	0.34
	Levy (2004)	59	61	115	0.05
	Marioni (2016)	42	3807	8665	0.06
	Protas (2013)	56	73	76	0.18
	Sager (200)	53	204	248	0.05
	Xu (2009)	58	18	25	-0.24
Language	Donix (2010)	59	12	16	0.07
	Jorm (2007)	-	611	1571	-0.02
	Langbaum (2010)	55	11	16	-0.29
	Levy (2004)	59	61	115	0.10
	Marioni (2016)	42	3807	8665	0.05
	Protas (2013)	56	73	76	-0.14
	Sager (2005)	53	204	248	-0.12
	Xu (2009)	58	18	25	-0.18
Visuospatial	Casell (2011)	59	50	50	0.12
	Langbaum (2010)	55	11	16	-0.04
	Levy (2004)	59	61	115	0.04
	Protas (2013)	56	73	76	0.12
	Sager (2005)	53	204	248	-0.10
Processing speed	Blair (2005)	56	1720	3648	0.01
	Blair (2005)	56	698	744	-0.13
	Goveas (2013)	54	20	26	0.08

Jorm (2007)	-	611	1571	0.01
Levy (2004)	59	61	115	-0.11
Marioni (2016)	42	3807	8665	-0.01
Patel (2013)	45	14	22	0.33

Notes: Caucasians (C), Afro-Americans (A)

Table 3. A summary of findings for the meta-analysis within each cognitive domain.

Domain	Studies (k)	ε4+ ( <i>n</i> )	ε4- ( <i>n</i> )	d	95% CI	Q
Global	8	602	2315	0.09	01, .18	5.20
Memory	19	7702	15814	-0.01	04, .02	17.40
EA	12	2045	3615	-0.03	10, .03	8.60
VF	10	6869	13909	0.02	02, .06	8.17
Language	8	4797	10732	0	07, .07	6.81
Visuospatial	5	399	505	-0.01	14, .12	2.78
PS	7	6931	14791	-0.01	04, .02	7.15

Table 4. A summary of longitudinal studies investigating APOE differences in mid-adulthood

First Author (year)	n	Age: M (range)	Gender (% M)	Ethnicity	Cognitive domain	Neuropsychological tasks	Follow-up	Attrition	Genotype comparison					
D1.:. (2005)	(010	(010	6910	6810	6810	6810	56	51	6202 Caucasian		DWD DSS VE	6 yrs (2-yr	240/	<b>1.</b> ε2+ vs. ε3 vs. ε4 He vs. ε4 Ho (ε2/ε2; ε2/ε3
Blair (2005)	6810	(45-64)	38	1693 African- American	M, EA, VF	Dwk, D55, vf	intervals)	24%	vs. ε3/ε3 vs. ε2/ε4, ε3/ε4 vs. ε4/ε4) <b>2.</b> ε4- vs. ε4+					
Caselli (2009)	815	60 (21-97)	31	85% Caucasian, 12 % Latino, 3%	G, M, VF, VS	MMSE, AVLT, COWAT, JLO	5 yrs (1-2 yr intervals	-	ε4- vs. ε4+ (ε3/ε3, vs. ε3/ε4, ε4/ε4)					

Caselli (2011)	621	57 (21-97)	30	-	M, EA, VF	AVLT, COWAT, PASAT, DSS, WCST, Iowa Gambling task	6.3 yrs (2-yr intervals)	23%	ε4- vs. ε4+ (ε3/ε3, vs. ε3/ε4, ε4/ε4)
Greenwood et al (2005b)	139	60 (33-85)	31	-	M, EA	WMS-G, WMS-D, Cued Visual Search task	3 yrs (1-yr intervals)		<ul> <li>ε4- vs. ε4 He vs. ε4 Ho</li> <li>(ε2/ε2, ε2/ε3, ε3/ε3 vs.</li> <li>ε2/ε4, ε3/ε4 vs. ε4/ε4)</li> </ul>
Greenwood (2014)	249	(40-59)	-	97% White	G, M EA	MMSE, WAIS logical memory,WAIS letter- number sequencing, Delayed match-sample task	3 yrs (1-yr intervals)	-	ε4- vs. ε4+ (ε2/ε2, ε2/ε3, ε3/ε3 vs. ε2/ε4, ε3/ε4, ε4/ε4)
Jochemsen (2012)	188	57 (27-79)	80	-	G, M, EA, VF	RAVLT, ROCF, Elevator task, Brixton spatial task, MMSE, VF	3.8 yrs	44%	ε4- vs. ε4+ (ε2/ε2, ε2/ε3, ε3/ε3 vs. ε3/ε4, ε4/ε4)
Kozauer (2008)	492	53 (18-65)	-	-	G, M	MMSE, Immediate recall, Delayed recall, Recognition	22 yrs (3 follow-ups_	-	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Schultz (2008)	626	55 (50-59)	100	95.5% Caucasian, 3.8% African- American, 0.3% Hispanic, 0.3% "other."	G	AFQT	35 yrs	-	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4, $\epsilon$ 3/ $\epsilon$ 4, $\epsilon$ 4/ $\epsilon$ 4)
Zhao (2005)	1128	- (40-49)	77	European descent	G M VF L	Verbal memory, AH4-1, MHV_VF (letter	6 yrs	-	$\epsilon$ 4- vs. $\epsilon$ 4+ ( $\epsilon$ 2/ $\epsilon$ 2, $\epsilon$ 2/ $\epsilon$ 3, $\epsilon$ 3/ $\epsilon$ 3 vs. $\epsilon$ 2/ $\epsilon$ 4. $\epsilon$ 3/ $\epsilon$ 4
2003)	2601	- (50-59)	74	European descent	G, 111, 11, L	category)	6 yrs	-	ε4/ε4)

Other,

Abbreviations: Domain- Global (G), Memory (M), Executive ability (EA), Verbal Fluency (VF), Language (L) Visuospatial (VS). Tasks-Mini-Mental State Examination (MMSE), Weschler Adult Intelligence Scale (WAIS), Weschler Memory Scale (WMS), Delayed Word Recall (DWR), Rey's Auditory Verbal Learning Task (AVLT), Controlled Oral Association Task (COWAT), Digit-symbol Substitution (DSS), Paced auditory serial attention task (PASAT), Wisconsin Card-sort task (WCST), Armed Forces Qualification task (AFQT), Rey-Osterrich Complex figure (ROCF), Judgement of Line Orientation (JLO), Mill Hill Vocabulary test (MHV). Zygosity: Heterozygous (He), Homozygous (Ho).