GENOME-WIDE ASSOCIATION FINDINGS FROM THE BRAINS FOR DEMENTIA RESEARCH COHORT

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ABSTRACT:

The Brains for Dementia Research (BDR) cohort (~3200) is a longitudinal clinicopathological programme, complimented with genetic analysis for the purposes of aetiological investigation into dementia. Here the data from genetic association analyses are presented from the initial collection of DNA from the BDR cohort. The aim of this study was to investigate the preliminary association signals for pathologically confirmed Alzheimer's disease samples compared to controls with no other pathology (n=520). Genome-wide genotyping was carried out using the NeuroChip platform. Analysis utilised the standard PLINK software for association studies. Genome-wide Bonferroni significant association were observed on chr19 around the *APOE/TOMM40* locus across two distinct linkage disequilibrium blocks. Eleven of the top 35 association signals have been identified in previous studies, in addition to an intriguing SNP association within the *FPR1* gene locus. This study suggests the BDR is genetically comparable to other Alzheimer's disease cohorts and offers an independent resource to verify findings, and additional genetic data for meta-analyses.

Keywords. Alzheimer's disease, GWAS, *APOE, FPR1,* Brains for Dementia Research (BDR), NeuroChip

1. *INTRODUCTION:*

Genome-wide association studies are now standard in the pursuit of genetic risk factors for disease. In order to achieve high levels of statistical power to observe small effect sizes, many Alzheimer's disease cohorts have been combined to create such break-through investigations as the International Genomics of Alzheimer's Project (IGAP, Lambert et al., 2013). The Brains for Dementia Research (BDR, brainsfordementiaresearch.org.uk) project is a growing longitudinal cohort of controls and dementia samples. To date there are just under 1200 DNA samples collected from either blood or brain tissue and is projected to include ~3200 samples when complete, offering additional genetic information on a genome-wide scale. Brain tissue is collected, alongside serially administered clinical assessments, for research purposes from neuropathologically defined samples (Francis et al., 2018). The in-life assessments include measures of cognition, mood, behaviour, general health and lifestyle and occur every 1-5 years depending on age and cognitive status. All such data is available through the Dementias Platform UK (DPUK, https://portal.dementiasplatform.uk). An extensive neuropathological examination of each brain at post-mortem provides diagnosis and full details of multi-morbidities according to standard criteria. Data for deceased participants is available through the Medical Research Council (https://mrc.ukri.org/research/facilities-and-resources-for-researchers/brain-banks/).

Previously we have published results from exome-sequencing, established AD SNP associations and polygenic risk score analysis using the BDR samples (Brookes et al., 2018; Chaudhury et al., 2019; Patel et al., 2017). This investigation details the genome-wide analysis of this initial collection of the BDR cohort using the NeuroChip (Blauwendraat et al., 2017) for which, the data is freely available for additional research via the DPUK. We present the results of our genome-wide association analysis to extend our previous analysis on established GWAS hits (Brookes et

al., 2018) demonstrating the utility of this data, its consistency with other genome-wide datasets for Alzheimer's disease and novel findings for further exploration.

2. *MATERIALS & METHODS:*

2.1 Samples:

The DNA bank for the BDR brain cohort currently has a total of 789 samples consisting of various dementia subtypes (AD, FTLD, VAD, LBD, Mixed, MCI) and controls with and without non-dementia neuropathology (e.g. Parkinson's); 93.3% (n=736) of this sample has been successfully genotyped on the NeuroChip platform. The genotyped cohort includes 359 confirmed as AD as the primary dementia (age at onset >65 years) cases and 175 cognitively normal controls without additional neuropathology; all diagnoses were neuropathologically confirmed.

2.2 DNA Extraction:

DNA was extracted from brain tissue using standard phenol-chloroform procedures. Samples were analysed on the Agilent TapeStation and quantified using the Nanodrop 3300 spectrometer to ensure high concentration and quality material was obtained.

2.3 Genotyping:

The NeuroChip is a custom Illumina genotyping array with an extensive genome-wide backbone (n=306,670 variants) and custom content covering 179,467 variants specific to neurological diseases (Blauwendraat et al., 2017). There are 284 variants on the NeuroChip that are specific to AD, including 10 of the 19 initial GWAS index SNPs (Lambert et al., 2013). When this database was created, the Lambert et al study was the most influential publication at the time and therefore we sought to genotype these GWAS index SNPs not included on the NeuroChip panel (n=9). We

continued this genotyping over the years for consistency, carried out by 'in-house' using KASP assays and following standard protocols (LGC, Middlesex), as previously described in the publication focusing on these SNPs (Brookes et al., 2018). KASP assay genotypes calls were confirmed using several samples with Sanger sequencing. Samples were also genotyped for *APOE* ε2, ε3 and ε4 alleles using the TaqMan assay for SNPs rs7412 and rs429358 (Applied Biosystems) to determine *APOE* status. The genotype data for the BDR cohort is available on the Dementia Platform UK upon request (https://www.dementiasplatform.uk/).

Quality control of the NeuroChip was completed in GenomeStudio (version 2.0, Illumina) and PLINK v1.9 (Purcell et al., 2007). Manual curation of the SNP clustering performed by Genome Studio algorithms was conducted on all SNPs. SNPs with ambiguous clustering of the three genotypes were removed. Likewise, individual sample signals which lay ambiguously between genotype clusters were also removed. Duplicate samples had a concordance rate of >0.999. Average GenTrain score, cluster separation and SNP call frequency were 0.83; 0.85 and 0.996 respectively in the exported PLINK compatible files. Genotype data was aligned to the GRCh37/hg19 reference genome.

Further quality control for the 359 AD and 175 controls without further neuropathology utilised in this investigation was conducted using PLINK v1.9 (Purcell et al., 2007) and following previously described steps (Chaudhury et al., 2019; Guo et al., 2014; Marees et al., 2018). Briefly, SNPs with a minor allele frequency of less than 1%, had genotype calls of less than 95% and had control samples that significantly deviated from Hardy-Weinberg Equilibrium ($p<0.0001$) were removed. Samples that had less than 95% call rate were also removed. This resulted in a final analysis file of 520 samples (356 AD and 164 controls) and 283,464 variants with an average genotyping rate

of 99.9%. The average age at death was 83.2 (±8.5) years for AD samples and for control individuals the average age at death was 85.7 (±9.7) years demonstrating a significant increase in age at death for the controls (p=0.003). The proportion of females (48% and 55.5% respectively) suggests a higher percentage of females in the control group but is not statistically significant (p=0.131). Ancestry for this cohort was previously confirmed to be of "White European" ethnicity from Principle Component Analysis (Chaudhury et al., 2019).

2.4 Statistical Analysis:

Association analysis was carried out in PLINK v1.9 (Purcell et al., 2007), using Fishers exact test for allelic association, which although is conservative it guards against type I error in small samples such as this, especially for variants with low minor allele frequencies (Bush and Moore, 2012). Post-hoc clumping of the association results was carried out with the command –clump using the 1000 genomes of European descent dataset (Auton et al., 2015) for linkage disequilibrium (LD) structure. Parameters for clumping were as follows: clump-p1 0.05, clump-p2 1, clump-r2 0.8 and clump-kb 250. The most significant findings were then subjected to the more commonly applied logistic association analysis to incorporate known covariates for AD (sex, age at death and number of APOEε4 alleles). Further investigation of the *APOE/TOMM40* region LD structure was conducted using both the 1000 genomes data set and BDR cohort in Haploview (Barrett et al., 2005) using a 120kb region around the *APOE/TOMM40* locus significant associations and conditional testing for independent effects using PLINK v1.9 (Purcell et al., 2007). SNP lists were annotated with gProfiler SNPense (Raudvere et al., 2019).

3. ***RESULTS:***

The BDR sample is a growing cohort, with DNA available for over 1000 living and post-mortem samples for scientific use. The genetic analysis presented here consists of the current neuropathology-confirmed diagnosed sample, of 356 AD samples and 164 control samples, for which a higher proportion of female samples and a higher age of death were observed in the control sample and a higher proportion of *APOE* ε4 positive samples was observed in the AD group (Table 1).

INSERT TABLE 1 HERE

Results of the association analysis observed seven SNPs that were significant at the genome-wide level ($p< 5x10^{-8}$). All were located with 25kb of the *APOE* isoform index SNPs (rs429358 & rs7412) on chromosome 19, and indicated on the Manhattan plot in Figure 1, with details of these SNPs in Table 2. Five more SNPs from chromosome 19, 12 and 5 were found to be suggestive of significance with P-values of less than 0.00001. Forty SNPs were significant at the 0.0001 threshold and 12,715 SNPs were found to have a P-value $\leqslant$0.05. Full association results can be found in the supplementary material Table 1.

INSERT FIGURE 1 HERE

INSERT TABLE 2 HERE

The most significant finding was variant rs769449 on the NeuroChip, which is located in the coding region of *APOE* (chr19:45410002) only 1939bp away from rs429358 one of the two index SNPs that make up the *APOE* isoform, which was the fourth most significant SNP (Table 2). This region of the genome has a total of 19 SNPs that were suggestive of association with AD within

a 120kb region. Inspection of the linkage disequilibrium (LD) of this region using the software Haploview indicates that these association signals may be from two distinct blocks of moderate to high correlation present in both the BDR and 1000 genomes population datasets (Figure 2). Further investigation of association using conditional testing (--chap --independent-effect) indicates that the association with rs6589 located at the 3' end of the suggestive independent block may be tagging the *APOE* signal as no evidence of an independence was observed (p=0.545). However, those present in the 5' end of this block could not be analysed due the haplotype models being identical.

INSERT FIGURE 2 HERE

Correlation between SNP markers in genome-wide analysis can often result in numerous association signals being detected from the same LD block, therefore the association results were subjected to 'clumping' in PLINK to group together those SNPs that represent the same LD block and are indexed by the most statistically significant SNP. A r^2=0.8 was used to clump the SNPs together, based on the LD structure of genotyping information from the 1000 genomes project (Auton et al., 2015). This resulted in four SNPs independently associated with AD with genome-wide significance, with SNP rs34342646 as the index SNP for the LD block containing SNPs rs3432646-rs71352238-rs34404554. Variant rs769449 was not present in the 1000 genomes data and therefore was excluded from this analysis and subsequent clumping analysis.

Clumping of the data identified 35 LD-independent SNPs as having suggestive association with significance values of under 0.0001, and 11,040 SNPs with P-values of ⩽0.05. These SNPs did not show any significant differences for genotype missingness between cases and controls, data for the entire SNP dataset missingness can be found in Supplementary Table 2. Seven of these

top LD-independent 35 are on chromosome 19, with six within the 500kb region around the *APOE* gene (Table 3) Due to the known association of the number of *APOE* ε4 alleles, higher age at death and being female with AD, these covariates were controlled for in a logistic regression. Neither age at death nor sex were found to significantly add to the model, however the presence of *APOE* ε4 alleles were highly significant (P-value ⩽0.000612). All 35 LD-independent SNPs retained nominal significance with P-values of less than 0.05 (Table 3). SNPs located in known associated genes with AD were identified, including *APOE, TOMM40, NECTIN1* and *APOC1,* alongside more novel genes.

The top 35 LD-independent SNPs were compared to existing summary statistics from the IGAP and Jansen et al studies (Jansen et al., 2019; Lambert et al., 2013), finding that 11 of these variants were also identified as significantly associated in both cohorts albeit not the same SNPs in each (Table 3), with the same effect allele identified in all cases. Subsequent comparisons with the IGAP combined cohort and follow-up investigation by Kunkle et al (2019) were not possible due to these SNPs not being included in their analyses. Further exploration of all SNPs observed to have P-values of nominal significance (P⩽0.05) with existing large GWAS cohorts found that 53 SNPs in both the Kunkle (Kunkle et al., 2019) and IGAP (Lambert et al., 2013) summary statistics supported the current findings, with 31 of these SNPs also supported by the Jansen et al study (Jansen et al., 2019) (Supplementary Table 3). All findings on chromosome 19 (n=6) were in concordance with the data from IGAP, along with rs246173 & rs246185 near the *MIR193BHG* gene on chromosome 16, rs141776877 (chromosome 13), rs73210863 (chromosome 8) and rs12286561 (chromosome 11).

INSERT TABLE 3 HERE

4. *DISCUSSION:*

The BDR cohort is a growing cohort and although it is insufficiently powered to detect some of the previously identified GWAS SNPs of small effect size, this dataset is demonstrating some unique association signals that may important.

Comparisons with other large GWAS datasets (Jansen et al., 2019; Kunkle et al., 2019; Lambert et al., 2013) show there are 53 nominally significant (P-value ≤0.05) SNPs in common, suggesting the BDR will be a crucial independent dataset for use in verifying findings, such as polygenic risk scores that primarily use the amalgamated dataset of IGAP.

4.1 APOE/TOMM40 region:

The association of the rs429358 identified in this study is a long-established risk factor for AD, and is thought to be responsible for the numerous association signals that are consistently observed across cohorts in and around the *APOE/TOMM40* region (Tanzi, 2012). The beta effect sizes the SNPs responsible for the APOE isoform (rs429358 & rs7412) are slightly larger in the BDR than that of the IGAP (rs429358 1.443 vs 1.350 and rs7412 -0.548 versus -0.387), which would be expected from a pathologically diagnosed cohort. The investigation of LD within this region in this study might suggest the presence of two independent association signals: one across the *APOE, TOMM40 and APOC1* genes and a second across the *NECTIN2/PVRL2* gene.

Huentelman et al (2010) observed the *TOMM40* SNP rs1160985 to be significantly associated with AD (as in this cohort), in samples who were of the *APOE* ε3/ε3 genotype leading them to suggest that the association of the SNP and perhaps even *TOMM40* was independent of *APOE*. However, the LD structure between rs1160985 and rs429358 in this dataset suggests that

although the SNPs have an r^2 of 0.14, suggesting that are weakly linked they are part of a much larger LD block which would infer that the signals are not fully independent. This extended linkage disequilibrium block encompasses 14 SNPs, of which 12 indicated association in this study (P-value ⩽0.05) and extends from the 3' end of *NECTIN2/PVRL2*, *TOMM40* into the *APOC1* gene downstream to *APOE*.

The *NECTIN2/PVRL2* gene locus extends over 36kb with seven SNPs observed to indicate association with AD in this study. Six of these signals are at the 5' end of the gene with a single association at the 3' of the gene. There appears to be significant LD breakdown in the middle of the gene, possibly indicating an independent association signal. The 3' end SNP rs34342646 appears to be in the same LD block as the *APOE* rs429358 SNP with a moderate r^2 value of 0.43; whereas those in the 5' region of the gene are in a separate cluster of association, supporting observations in recent literature (Rao et al., 2018; Zhou et al., 2019). However conditional haplotype analysis for independent effects does not support this, along with the SNPs showing nominal significance in *NECTIN2* in this study lacking support from larger GWAS cohorts (Jansen et al., 2019; Kunkle et al., 2019; Lambert et al., 2013).

4.2 Concordance with previous work:

Comparison of the findings presented in this study with summary statistics obtained from previous studies yielded mixed results. The top 35 SNPs observed in this study, had 33 of them genotyped in the IGAP discovery sample but were not genotyped the subsequent combined cohort or the follow-up study with greater sample sizes (Kunkle et al., 2019; Lambert et al., 2013); the Jansen et al study did include genotyping for 34 of these SNPs (Jansen et al., 2019). In both the IGAP stage 1 and Jansen data 11 of the 35 SNPs were also found to demonstrate nominal significance, though these were not in complete concordance between the studies.

Fifty-three SNPs that were indicative of association in the BDR (P-value ⩽0.05) were also observed to demonstrate a level of association in the IGAP cohorts and Kunkle summary statistics, with 31 supported by the summary statistics from Jansen (Supplementary Table 2). This includes multiple SNPs in previously associated genes for AD, *BIN1* and *MS4A4A*, but not the index SNPs identified in the Lambert et al study (2013). Exploration of these SNPs indicated that none were significantly associated in this cohort, with the closest trend indicative of association (P-value = 0.08) observed only with SNP rs17125944 linked with the *ZCWPW1* gene.

4.3 Support of Novel Association signals

One intriguing association signal in this study, previously observed with nominal significance (P=0.025) in the Jansen et al study (Jansen et al., 2019), but was not genotyped in the IGAP studies (Kunkle et al., 2019; Lambert et al., 2013), is the SNP rs4802859 on chromosome 19 almost 7Mb away from the *APOE/TOMM40* locus residing within the formyl peptide receptor 1 (*FPR1*) gene (Murphy et al., 1993).

The SNP identified in this study lies upstream of the *FPR1* gene, and has been found to regulate the genes expression in the brain; with the A-allele that was identified as having a protective effect in this study associated with lower gene expression (https://gtexportal.org/home/snp/rs4802859). The SNP rs4802859 also lies 5' to the *FRP2* gene, for which a rare copy number variant within the locus was found in a sporadic early onset (<55 years of age) Alzheimer's patient (Rovelet-Lecrux et al., 2012). Further to this exploration of the summary statistics of the IGAP studies found a SNP (rs4802861) located 3.3kb away from our finding within the *FRP1/FRP2* locus to demonstrate association across all three IGAP analyses (Stage 1 p=0.0009, Combined p=0.0007 and Kunkle p=0.007) (Kunkle et al., 2019; Lambert et al., 2013).

The FPR1 G-coupled cell surface receptor is thought to play a key role in neuroinflammation being highly expressed in immunocompetent cells in the brain. An in-depth review of this receptor and its potential role in neurodegeneration has recently been published (Trojan et al., 2019), but briefly neurodegenerative diseases are thought to be a result of chronic inflammatory process, through the disruption of mechanisms behind the resolution of inflammation; with the formyl peptide receptor family being key mediators in this process. Further to this amyloid-beta 1-42 (Aβ1-42) is known to activate glia cells, which release numerous proinflammatory signals leading to neurodegeneration (Heppner et al., 2015). *In vitro* studies have demonstrated that the Aβ activation of microglia cells can operate through the formyl peptide receptor family (Brandenburg et al., 2010) along with a broad spectrum of other ligands (He and Ye, 2017). Further to this, *Fpr1* expression in APP/PS1 transgenic mice has been shown to be altered (Slowik et al., 2012), with treatment of these mice with an antagonist for the receptor leading to beneficial effects on the cognitive phenotype (Schröder et al., 2020).

Combined, these studies support further investigation into this gene family with additional functional SNP mapping across the *FRP* locus complimented with translational studies to explore the potential of these receptors as a potential pharmacological intervention point for Alzheimer's disease (Chavan et al., 2017; Cussell et al., 2020; Doens and Fernández, 2014; Siracusa et al., 2019).

In conclusion, this study demonstrates the utility of the BDR as an independent cohort to international collections of data, and potential to identify novel genetic associations for further investigation.

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Brains for Dementia Research has ethics approval from London – City and East NRES committee 08/H0704/128+5 and has deemed all approved requests for tissue to have been approved by the committee.

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Conflict of Interest:

The authors have no conflict of interest to report.

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Table 1: Demographics of BDR samples analysed, indicating an increase in age at death and proportion of females in the control group, though only the age of death is statistically significant. Additionally, the proportion of *APOE* ε4 positive samples is significantly higher in Alzheimer's disease cases than controls.

	AD (n=356)	**Control (n=164)**	**P-value**
Average Age at Death (years (SD))	83.2 (±8.5)	85.7 (±9.7)	**0.003**
Percentage of females	48%	55.5%	0.131
Percentage of APOE ε4 positive	69.8%	32.2%	**<0.00001**

Figure 1: Manhattan plot of association results for the BDR cohort, indicating the most signficant SNP associations are located on chromosome 19, with the dots representing each SNP postined above the red line indicating genome-wide significance (n=7). A further 5 SNPs were found to suggestive of an association with significance of less than 0.00001 (blue line).

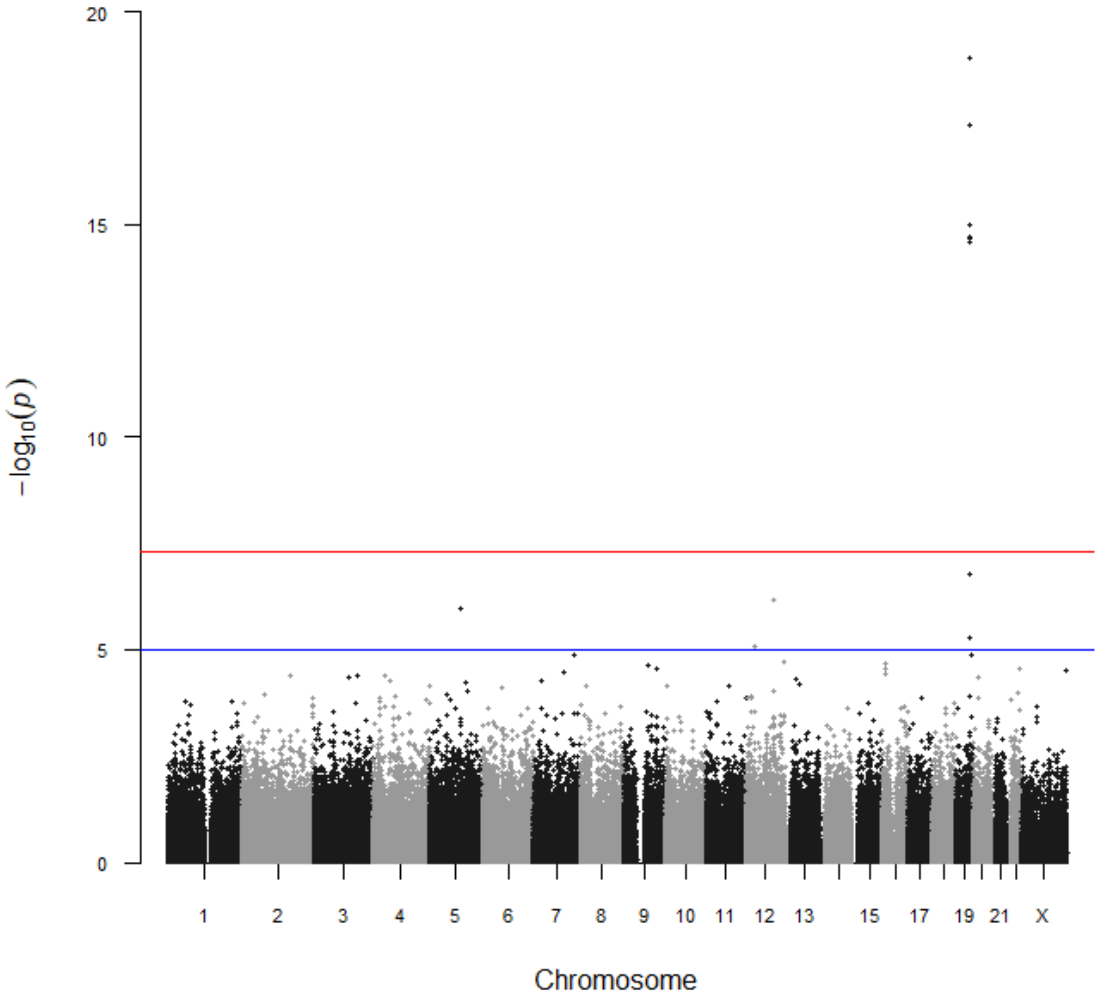
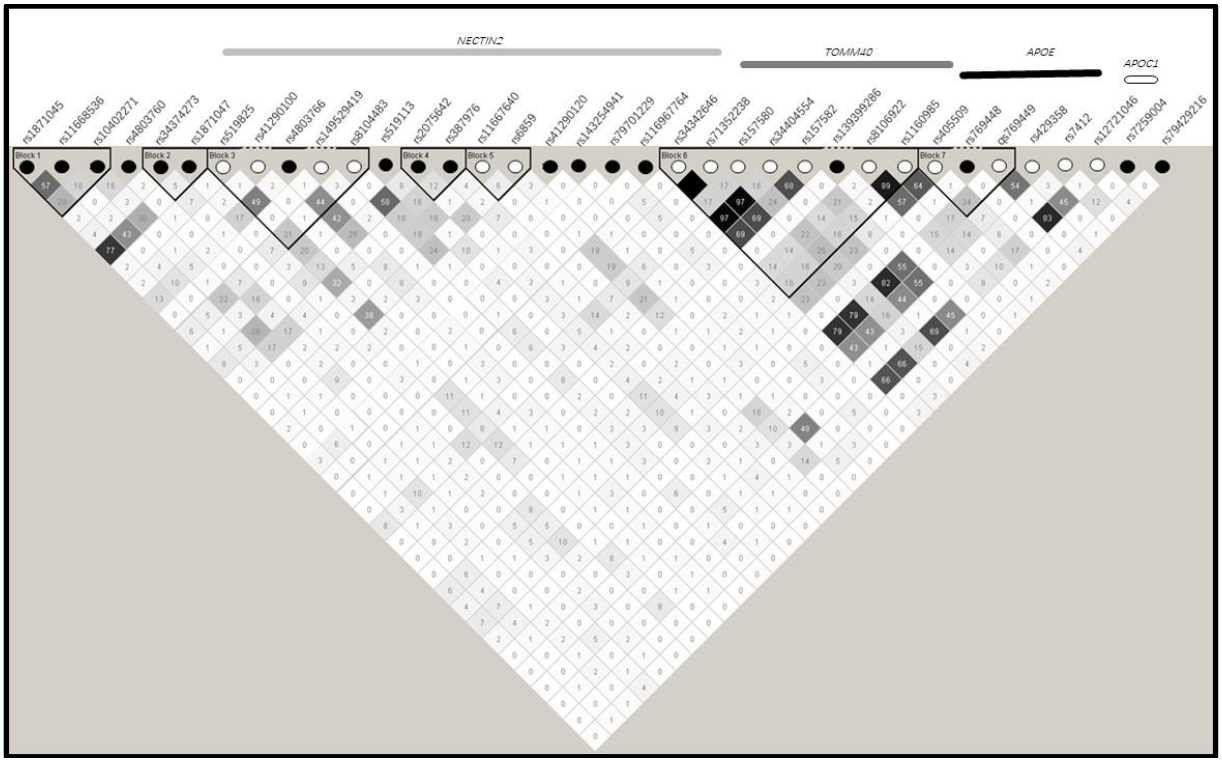


Table 2: Association results of the SNPs that surpassed genome-wide significance in the current BDR cohort. All seven variants were located on chromosome 19 and within a 25kb region surrounding the *APOE* gene locus. Minor allele frequency (MAF), odds ratio (OR).

SNP ID	Chr	bp	Minor Allele	MAF Cases	MAF Controls	P-value	OR
rs769449	19	45410002	A	0.3183	0.07622	1.2E-19	5.659
rs157582	19	45396219	A	0.4085	0.1463	4.4E-18	4.028
rs12721046	19	45421254	A	0.3404	0.1135	1E-15	4.031
rs429358	19	45411941	C	0.4113	0.1677	2E-15	3.467
rs34342646	19	45388130	A	0.323	0.1037	2.1E-15	4.126
rs71352238	19	45394336	G	0.323	0.1037	2.1E-15	4.126
rs34404554	19	45395909	C	0.3188	0.1006	2.6E-15	4.184

Figure 2: Haploview r^2 linkage disequilibrium plots derived from genotype data from the BDR cohort (top panel) and 1000 genomes of European descent (bottom panel) of the *APOE* region encompassing 118749bp around two clusters of significant association signals. In the top panel, the linkage disequilibrium suggests that SNPs with association significance of $\leqslant 0.05$ (white circles) fall into two distinct blocks separated by a region of extreme low linkage disequilibrium. The bottom panel derived from the 1000 genome data displays a similar linkage disequilibrium pattern across the region with comparable r^2 measures as the BDR Alzheimer's disease case-control cohort.



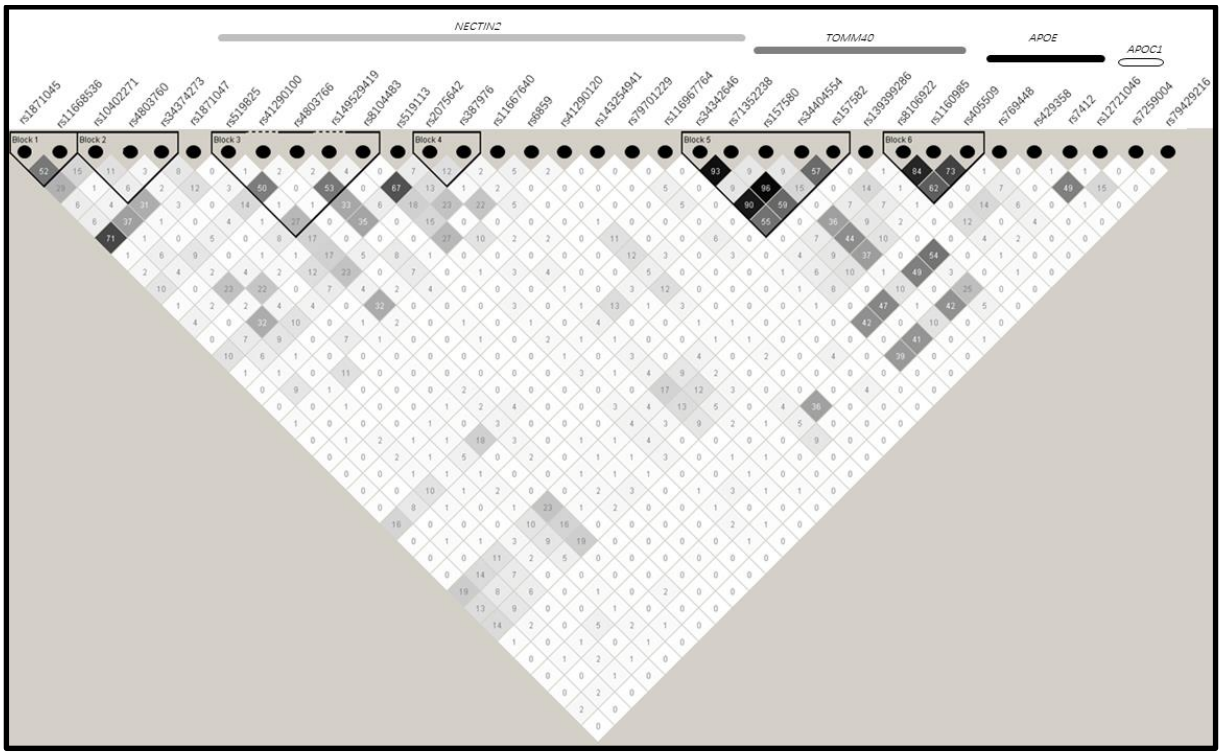


Table 3: Comparison of the top 35 LD-independent association results (after clumping) from the BDR cohort after controlling for covariates (age at death, sex and number of *APOE* ε4 allele), alongside results obtained from the IGAP stage 1 association study. Eleven variants that were observed in the BDR cohort were also identified to be significant (P≤0.05) in the IGAP cohort, and are in italics (Lambert et al., 2013).

SNP	Position	BDR Effect-Allele	BDR P-value	Co-variate adjusted P-value	SNPs in LD	Nearest Gene	IGAP Effect-Allele	IGAP P-value
rs157582	*19:45396219*	*A*	*4.38E-18*	*4.58E-04*		*TOMM40*	*A*	*9.70e-434*
rs12721046	*19:45421254*	*A*	*1.01E-15*	*8.57E-04*		*APOC1*	*A*	*1.05e-421*
rs429358	*19:45411941*	*C*	*1.97E-15*	-		*APOE*	*C*	*6.70e-536*
rs34342646	*19:45388130*	*A*	*2.07E-15*	*1.67E-03*	*rs71352238, rs34404554*	*NECTIN2, AC011481.2*	*A*	*4.93e-440*
rs157580	*19:45395266*	*G*	*1.59E-07*	*1.02E-02*		*TOMM40*	*G*	*1.21E-101*
rs9971898	12:92875607	C	6.89E-07	3.29E-06		*LINC02397, AC063949.2*	C	0.9904
rs13164188	5:103914523	G	1.10E-06	1.06E-05		*AC099520.1*	G	0.1388
rs6859	*19:45382034*	*A*	*5.27E-06*	*2.69E-02*		*NECTIN2*	*A*	*3.31E-96*
rs1258275	12:30706597	G	8.17E-06	1.04E-05			G	0.3618
rs10257276	7:136370812	A	1.28E-05	7.98E-04		*AC009264.1*	A	0.7525
rs4802859	19:52255196	A	1.38E-05	1.16E-04		*FPR1*	-	-
rs7953586	12:131217685	G	1.87E-05	1.14E-04			G	0.5254
rs246173	*16:14379836*	*G*	*2.04E-05*	*4.01E-04*	*rs30242*		*G*	*0.001343*
rs149105542	9:83764621	A	2.35E-05	3.27E-03			-	-
rs11794020	9:111899198	A	2.76E-05	9.81E-05		*FRRS1L*	A	0.8346
rs246185	*16:14395432*	*G*	*2.86E-05*	*1.08E-04*		*MIR193BHG*	*G*	*0.003725*
rs5768412	22:48567467	A	2.92E-05	2.19E-05			A	0.5012
rs740309	7:105456869	G	3.38E-05	1.01E-04		*ATXN7L1*	G	0.7444
rs16844790	2:160968628	G	3.87E-05	1.24E-04		*ITGB6*	G	0.3863
rs78019248	*3:148656332*	*G*	*3.91E-05*	*8.14E-04*		*AC092979.1, AC092979.2*	*G*	*0.05114*
rs6447103	4:41657672	A	4.21E-05	1.72E-04		*LIMCH1*	A	0.6684
rs7628485	3:118913337	G	4.29E-05	1.25E-03		*UPK1B*	G	0.3078
rs4814978	20:20530564	A	4.49E-05	2.18E-04		*RALGAPA2*	A	0.5853
rs17051917	13:35768789	A	4.92E-05	6.94E-05		*NBEA*	A	0.551
rs6842825	4:57125176	A	5.31E-05	2.57E-03		*CRACD*	A	0.4031

rs10480067	7:28064698	G	5.37E-05	8.53E-05		*JAZF1*	G	0.8878
rs17151277	5:123502228	A	5.62E-05	1.18E-03		*LINC01170*	A	0.1992
rs141776877	*13:50111581*	*A*	*6.62E-05*	*1.34E-04*		*RCBTB1*	*A*	*0.03703*
rs12570234	10:5382676	C	6.79E-05	5.59E-04			C	0.3367
rs1563455	4:190293157	A	6.87E-05	1.49E-03	rs11943937		A	0.3591
rs73210863	*8:19953027*	*A*	*7.00E-05*	*2.96E-03*		*AC100802.1*	*A*	*0.008712*
rs12286561	*11:80119435*	*A*	*7.31E-05*	*5.71E-04*			*A*	*0.0409*
rs9445788	6:67589752	G	7.94E-05	4.18E-04			G	0.87
rs9285919	5:129759493	G	9.08E-05	1.80E-04			G	0.1617
rs2431014	12:96084180	G	9.49E-05	5.90E-04		*NTN4*	G	0.8704