Journal of Human Genetics (2015) 60, 455–460

www.nature.com/jhg

ORIGINAL ARTICLE

GWA meta-analysis of personality in Korean cohorts

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Personality is a determinant of behavior and lifestyle that is associated with health and human diseases. Despite the heritability of personality traits is well established, the understanding of the genetic contribution to personality trait variation is extremely limited. To identify genetic variants associated with each of the five dimensions of personality, we performed a genome-wide association (GWA) meta-analysis of three cohorts, followed by comparison of a family cohort. Personality traits were measured with the Revised NEO Personality Inventory for the five-factor model (FFM) of personality. We investigated the top five single-nucleotide polymorphisms (SNPs) for each trait, and revealed the most highly association with neuroticism and *TACC2* (rs1010657, $P = 8.79 \times 10^{-7}$), extraversion and *PTPN12* (rs12537271, $P = 1.47 \times 10^{-7}$), openness and *IMPAD1* (rs16921695, $P = 5 \times 10^{-8}$), agreeableness and *RPS29* (rs8015351, $P = 1.27 \times 10^{-6}$) and conscientiousness and *LMO4* (rs912765, $P = 2.91 \times 10^{-6}$). It had no SNP reached the GWA study threshold ($P < 5 \times 10^{-8}$). When expanded the SNPs up to top 100, the correlation of *PTPRD* (rs1029089) and agreeableness was confirmed in Healthy Twin cohort with other 13 SNPs. This GWA meta-analysis on FFM personality traits is meaningful as it was the first on a non-Caucasian population targeted to FFM of personality traits.

Journal of Human Genetics (2015) **60,** 455–460; doi:10.1038/jhg.2015.52; published online 21 May 2015

INTRODUCTION

Personality traits determine social, behavioral and health outcomes of the individual.[1–7] Among methods to assess personality, the Revised NEO Personality Inventory (NEO PI-R), designed to characterize the five-factor model (FFM) based on neuroticism, extraversion, openness, agreeableness and conscientiousness, is the most practical and applicable method that provides a broad description of personality.[1,8]

Biologically, personality is a genetic phenotype with moderate heritability. In family, twin and adoption studies, each of the FFM personality dimensions is heritable, with broad-sense heritability estimates ranging between 33 and 65%.[1,9–16] Because genome-wide association (GWA) studies have been successful in investigating the association of common genetic variants with phenotypes, personality has been the focus of several GWA studies.[17–24]

A couple of Caucasian GWAS were conducted on personality traits using different measures, such as Eysenck Personality Questionnaire, NEO PI-R and the temperament and character inventory.[25–28] Most of these studies reported either GWA results were unreplicated or the associations identified that genetic variants did not significantly associate with personality. In previous study, we identified and confirmed a novel region on *OR1A2* (olfactory receptor, family 1, subfamily A, member 2) was associated with neuroticism in the GWAS on personality for the first East-Asian population.[9]

To increase the statistical power of the analysis, researchers would combine the results from multiple cohorts into a single meta-analysis.[22,29,30] A few meta-analyses of GWAS on personality traits using NEO PI-R or temperament and character inventory have previously been performed. de Moor *et al.*[1] revealed significant associations for openness near *RASA1* (RAS p21 protein activator 1) and for conscientiousness within *KATNAL2* (katanin p60 subunit A-like 2) in a study including 17 375 discovery and 3294 replication samples. Terracciano *et al.*[17] identified common variants in *CTNNA2* (catenin cadherin-associated protein, alpha 2 gene) associated with excitement-seeking (7860 samples of Caucasian ancestry). Using the temperament and character inventory, Service *et al.*[31] revealed several genes associated with the four temperament dimensions including *PTPRD* (protein tyrosine phosphatase, receptor type, D) and persistence, but these results were not statistically significant (>11 000 populations). Accordingly, large-scale collaborative studies are still difficult to replicate and do not yet adequately explain the heritability of these complex traits.

Any reports for GWA meta-analyses on personality were lacking compared with analyses for other complex traits, especially for Asian

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Received 12 December 2014; revised 6 March 2015; accepted 8 April 2015; published online 21 May 2015

Table 1 Genotyping information of the four studies participating in this meta-analysis

Cohort	*Total (n)*	*Male (n)*	*Female (n)*	*Age (mean ± s.d.)*	*Genotyping platform*	*Pre-imputed SNPs*	*Imputed-SNPs*	*Post-qc[a] SNPs*
Ansung	1126	490	636	62.47 ± 8.27	Affymetrix	500 568	1 387 466	778 706
Ansan	1683	825	858	57.03 ± 6.77	Affymetrix	500 568	1 387 466	778 706
Young women	1089	—	1089	26.14 ± 4.66	Illumina	625 112	1 581 609	1 142 174
Healthy twin	1021	425	596	43.46 ± 14.09	Affymetrix and Illumina	514 643 and 186 965	26 069 070	4 624 402

[a]Post-qc was quality-control analyses after imputation, which filtered out poorly imputed SNPs with info from IMPUTE2 under 0.7 and minor allele frequency under 0.01.

populations. These researches have been conducted almost exclusively in Caucasian populations, and the results were hard to duplicate. The goal of this study is to identify meaningful genetic variants of the FFM personality dimensions by combining GWA results from three Korean cohorts and confirmed the replications in the family cohort.

MATERIALS AND METHODS

Description of samples

Total 4919 subjects were included in this study. All cohorts were reviewed and approved by local institutional review boards, and written informed consent was obtained. The rural Ansung (1126 participants, male 490, female 636, age range 49–80, mean 62.47, s.d. 8.27) and urban Ansan (1683 participants, male 825, female 858, age range 46–79, mean 57.03, s.d. 6.77) cohorts are two community-based cohorts, which are part of the Korean Association Resource phase 3, initiated in 2007. Detailed protocols and characteristics of study participants have been described previously.[32,33] All subjects included in this study had valid scores on the NEO PI-R and were genotyped using Affymetric Genome-Wide Human array 5.0 (Affymetrix, Inc., Santa Clara, CA, USA).

The Young Women cohort in Korea was initiated in 2008. This cohort included samples from 2000 Korean women aged 18–40 years (mean 26.14, s.d. 4.66) whose genotype had been recorded. Among those, 1140 participants completed both the personality questionnaire and genotype testing. After completing quality-control procedures to eliminate invalid subjects, 1089 participants were included. This study is based on the data available from the Illumina Human 1M-Duo DNA Analysis BeadChip and BeadStudio software (Illumina Inc., San Diego, CA, USA).

Replication samples

The Healthy Twin study is a family-based cohort consisting of adult twin pairs and their first-degree family members. Detailed protocols and characteristics of study participants have been described previously.[34,35] The genotyping of Healthy Twin study samples was performed on either the Affymetrix Genome-Wide Human array 6.0 (Affymetrix, Inc.) or Illumina Infinium HumanCore-12 Beadchip (Illumina). This cohort consisted of 149 pairs of monozygotic twins and 24 pairs of dizygotic twins with their family. Among these 1170 participants, only one of the monozygotic twins was randomly included in the analysis for this study (total 1021 participants, mean aged 43.36 ± 14.09).

Genotyping and imputation

Genomic DNA was extracted from whole-blood samples using a commercial isolation kit according to the manufacturer's protocols. Genotyping was performed using Illumina or Affymetrix mapping array sets, as noted above for each cohort. Standard quality screening was conducted independently in each cohort, in which all genotyped markers with a call rate of <0.95, minor allele frequency of <0.01, or out of Hardy–Weinberg Equilibrium ($P<0.001$) were filtered out. We used PLINK software[36] for the quality-control procedure and to identify duplicate samples or related individuals. After quality-control, we pre-phased to construct haplotypes of the autosomal chromosomes by SHAPEIT2[37] and subsequent imputation was performed by IMPUTE2[38] owing to different chip platforms. These studies used NCBI build 36 (UCSC hg18) and HapMap3 release 2 (JPT+CHB, 1.39 M), and Korean HapMap panel data (1.66 M) were combined to serve as the reference panel (Table 1). Before the meta-analysis, poorly imputed single-nucleotide polymorphisms (SNPs) with imputation quality $\leqslant 0.70$ (info from IMPUTE2) were filtered out, such that the final data set included ~1.0 M SNPs in each cohort. The genomic inflation factor (λ) of this study was under the 1.007 for all personality dimensions. We did not correct for genomic control in the GWA analyses, as inflation was modest and plots of multi-dimensional scaling and principle component analysis suggested that population structure might be disregarded for three cohorts (Supplementary Figure 1).

Personality assessment

Personality traits were assessed using the Korean short version of the NEO PI-R (PSI Consulting Corp., Seoul, Korea), which is a 90-item questionnaire designed to operationalize the FFM. The NEO PI-R has a robust factor structure that has been replicated in Korea[39] and in >50 other cultures.[40] The Korean version of the NEO PI-R has been used in the Korean population and has demonstrated good reliability and validity.[39] Internal consistency and reliability of this questionnaire was analyzed by Cronbach α. Values were 0.61–0.75 in the Ansung and Ansan cohorts, 0.75–0.88 in the Young Women cohort and 0.70–0.80 in the Healthy Twin study. The questionnaire consisted of 18 items per factor (that is, neuroticism, extraversion, openness, agreeableness and conscientiousness). Items were answered on a 5-point Likert-type scale, ranging from strongly disagree to strongly agree. Phenotype scores for the analysis were computed by summing up the six facets composing each factor after reversing negatively keyed items. According to the NEO PI-R manual, we analyzed item-response patterns and did not include invalid or missing responses in our data set.

Statistical analyses

Before association analyses, we calculated the heritability of each five personality dimension for population cohorts and family cohort by using the Genome-wide Complex Trait Analysis and GenABEL, respectively.[41,42] Each study independently performed single marker association analyses with personality using linear regression under an additive genetic model by PLINK program. Age and sex were used as covariates in each study. A meta-analysis of the results was performed by METAL[43] using the weighted inverse variance method, which is based on regression coefficients (β values), standard errors and its *P*-value by weighing the effect estimates of the individual samples by the inverse of variance and by taking into account the direction of effect. As METAL was only used for fixed-effects meta-analysis, a random-effect analyses were also implemented using GWAMA.[44]

Replication analyses

Healthy Twin cohort study independently performed single marker association analyses with personality. Using linear regression under an additive genetic model, analysis for this study was performed using PLINK. The Family-based Score Test for Association in the GenABEL package was also used in the R project for the statistical results after linear regression.[42] These sample were imputed based on 1000 Genome Asians, and SNPs in each sample controlled by Mendelian error 1% and info score 0.7, followed by cross-check of two platform, then checked for minor allele frequency, Hardy–Weinberg equilibrium and call rate as same as meta-analysis standards. The threshold of a $P<0.05$ was taken as significant evidence of replication.

RESULTS

Our meta-analysis on personality GWAS was conducted with a total of 3898 subjects by assembling three cohorts, and compared this result with the family cohort including 1021 participants. Before GWA meta-analyses, we calculated the heritability of each five personality

Table 2 SNPs with the strongest association (five SNPs with the lowest *P*-value) with each personality trait from the meta-analysis of GWAS

Factor	*SNP*	*Alleles*	*Beta*	*s.e.*	P-*value*	*Direction*[a]	*HetPVal*	*Chr*	*Position*	*Related gene*[b]	*Location*	*Replicated* P[c]
Neuroticism												
	rs1010657	C/T	−0.137	0.028	8.79E-07	−−−	0.184	10	123987707	*TACC2*	Intron	—
	rs11627869	A/G	0.119	0.027	8.81E-06	+++	0.651	14	76137067	*ESRRB*	Intergenic	0.808
	rs1676245	C/T	−0.117	0.027	1.26E-05	−−−	0.649	14	76137381	*ESRRB*	Intergenic	0.808
	rs2461923	C/T	−0.179	0.041	1.44E-05	−−−	0.525	10	20466206	*PLXDC2*	Intron	0.922
	rs10830242	C/T	−0.128	0.030	1.85E-05	−−−	0.312	11	87500294	*RAB38*	Intron	—
Extraversion												
	rs12537271	C/T	0.166	0.032	1.47E-07	+++	0.021	7	77138662	*PTPN12*	Intergenic	0.898
	rs577149	C/T	−0.175	0.035	4.15E-07	−−−	0.551	11	125977722	*KIRREL3*	Intron	0.944
	rs11761707	A/G	−0.159	0.033	1.44E-06	−−−	0.209	7	77076120	*PTPN12*	Intron	0.106
	rs6955503	C/T	0.157	0.033	1.62E-06	+++	0.223	7	77065177	*PTPN12*	Intron	0.117
	rs12113982	A/G	−0.161	0.034	1.73E-06	−−−	0.143	7	77014326	*PTPN12*	Intron	0.088
Openness												
	rs16921695	G/T	0.139	0.029	2.26E-06	+++	0.013	8	58220209	*IMPAD1*	Intergenic	0.272
	rs17194487	A/G	−0.153	0.033	2.8E-06	−−−	0.111	8	58267466	*IMPAD1*	Intergenic	0.737
	rs7818728	C/T	−0.140	0.030	2.95E-06	−−−	0.008	8	58262926	*IMPAD1*	Intergenic	0.308
	rs11992943	C/T	0.140	0.030	3.02E-06	+++	0.009	8	58291218	*IMPAD1*	Intergenic	0.326
	rs10876849	G/T	0.107	0.023	3.14E-06	+++	0.459	12	54343126	*OR10P1*	Intergenic	—
Agreeableness												
	rs8015351	A/G	−0.108	0.022	1.27E-06	−−−	0.180	14	48958135	*RPS29*	Intergenic	0.969
	rs7146832	A/C	−0.105	0.022	2.28E-06	−−−	0.204	14	48957073	*RPS29*	Intergenic	0.894
	rs746784	C/T	−0.147	0.032	3.21E-06	−−−	0.741	2	67124795	*DNMT3AP1*	Intergenic	0.282
	rs12880745	A/G	0.103	0.022	4.41E-06	+++	0.106	14	48973950	*RPS29*	Intergenic	0.964
	rs1420361	G/T	−0.130	0.028	4.83E-06	−−−	0.105	2	67119287	*DNMT3AP1*	Intergenic	0.402
Conscientiousness												
	rs912765	C/T	0.122	0.026	2.91E-06	+++	0.551	1	87416535	*LMO4*	Intergenic	0.448
	rs10471321	C/G	0.116	0.025	3.89E-06	+++	0.164	5	65676338	*SFRS12*	Intergenic	0.913
	rs13178223	C/T	0.115	0.025	4.75E-06	+++	0.152	5	65672811	*SFRS12*	Intergenic	0.988
	rs7727166	C/T	−0.114	0.025	5.33E-06	−−−	0.222	5	65676926	*SFRS12*	Intergenic	0.916
	rs912764	C/T	0.114	0.025	7.36E-06	+++	0.521	1	87416040	*LMO4*	Intergenic	0.450

Abbreviations: beta, regression coefficient; Chr, chromosome; s.e., standard error; HetPVal, heterogeneity *P*-value; position, base pair location; SNP, single-nucleotide polymorphism.
[a]Direction is described Ansan, Ansung and Young Women cohort in sequence.
[b]Related genes are defined as the closest gene to the SNP within the signal boundary or the closest gene within a 300-kb window.
[c]Replicated *P* is an association *P*-value of the Healthy Twin cohort.

dimension for each cohort. The heritability of personality traits was from 39 to 75% in population cohorts using the SNP-based method and it showed from 22 to 35% in twin family data (Supplementary Table 1). Most meta-analyses usually define *P*-value thresholds as 5×10^{-8}, but our SNPs for each personality trait were not presented significance. The *P*-values of the most top-ranked SNPs with a heterogeneity *P*-value (HetPVal) >0.05 ranged from 2.91×10^{-6} for conscientiousness to 1.47×10^{-7} for extraversion (Table 2). Among listed top five results using fixed-effects model, SNPs with HetPVal>0.1 were reanalyzed under a random-effects model and their significance was confirmed (Supplementary Table 2).

For neuroticism, the most meaningful SNP (rs1010657; $P=8.79\times10^{-7}$) was within *TACC2* (transforming acidic coiled-coil containing protein 2) (Figure 1a). The TACC proteins are a conserved family of centrosome- and microtubule-interacting proteins, and TACC2 is predominately expressed in the brain.[45] Both rs11627869 ($P=8.81\times10^{-6}$) and rs1676245 ($P=1.26\times10^{-5}$) were located within an intron of *ESRRB* (estrogen-related receptor beta), which encodes a protein with similarity to the estrogen receptor. Its function is not well established, but it is reported that it affects body composition, neuropeptide levels, stress hormones via hypothalamic-pituitary-adrenocortical axis and centrally-modulated startle responses.[46] The SNP rs2461923 ($P=1.44\times10^{-5}$), located near *PLXDC2* (plexin domain containing 2) on chromosome 10, was also associated with neuroticism. The PLXDC2 is a type I transmembrane protein with some homology to nidogen and to plexins, and is expressed in a highly discrete and dynamic pattern in the developing nervous system.[47]

For extraversion, the most associated SNP was rs12537271 ($P=1.47\times10^{-7}$) near *PTPN12* (protein tyrosine phosphatase, non-receptor type 12) (Figure 1b). This gene also related with other SNPs (rs11761707, rs6955503 and rs12113982) among the top five in extraversion. The protein encoded by *PTPN12* is a member of the protein tyrosine phosphatase family, which acts on signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle and oncogenic transformation. The SNP rs577149 ($P=4.15\times10^{-7}$), which maps to the intron of *KIRREL3* (kin of IRRE like 3), was also associated with extraversion. The protein encoded by this gene is a member of the nephrin-like protein family,

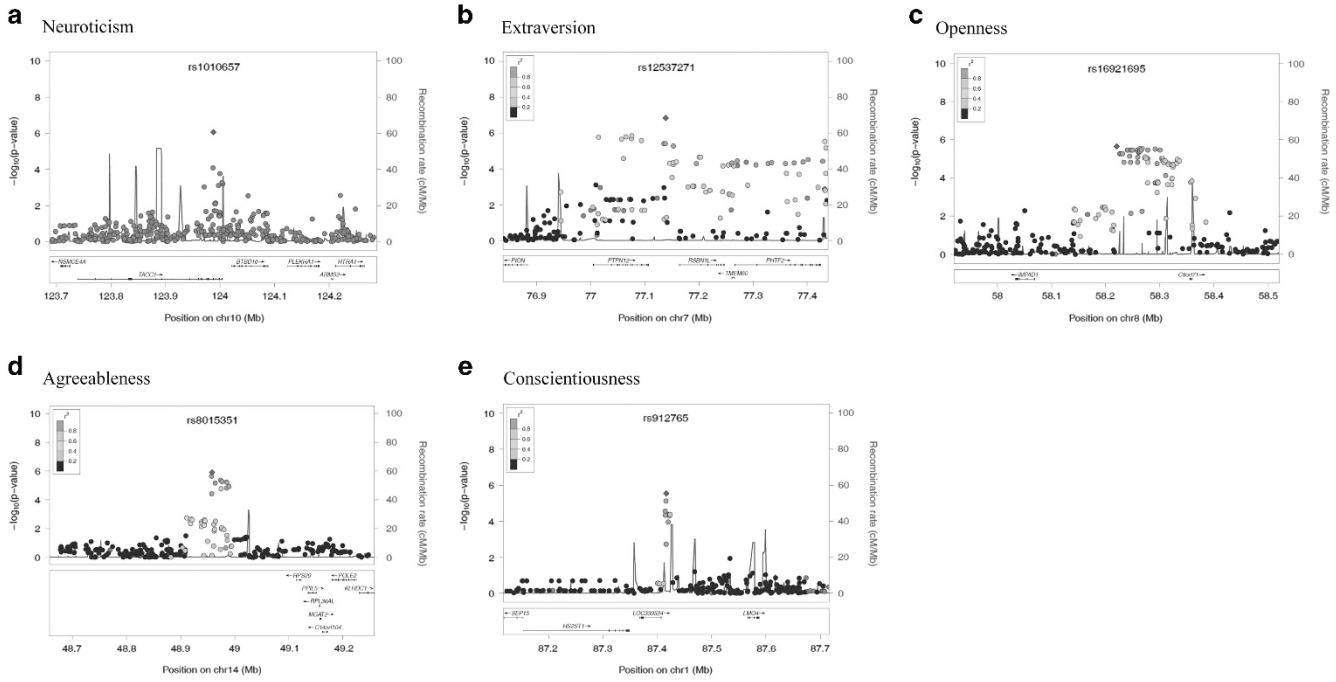

Figure 1 Regional association plots of top hits SNPs in the meta-analysis of three GWAS for FFM personality. Regional plots show association of *P*-values as the $-\log_{10}$ scale on the vertical axis and the chromosomal position along the horizontal axis. Panels show SNPs associated with neuroticism (**a**), extraversion (**b**), openness (**c**), agreeableness (**d**) and conscientiousness (**e**). A reference SNP (rs) number for the most significantly associated SNP (which exhibited the lowest *P*-value in each plots) is marked for each panel. SNPs are expressed as different colored circles, coded based on r^2 values, where SNP between 0.8–1 are red, 0.6–0.8 are yellow, 0.4–0.6 are green, 0.2–0.4 are light blue and <0.2 are dark blue. SNPs with missing LD information are shown in grey. Violet dots at each locus indicate the strongest signal detected in this meta-analysis of the genome-wide scan. The blue lines show the recombination rates given in the HapMap Phase II JPT+CHB. The genes listed below the plots indicate the RefSeq genes at the loci. The physical positions of SNPs and genes are based on NCBI genome build 36 (hg18). A full color version of this figure is available at *Journal of Human Genetics*'s website.

which is expressed in fetal and adult brain, and also in podocytes of kidney glomeruli.

Several openness-associated SNPs including the one having lowest *P*-value (rs16921695, rs17194487, rs7818728 and rs11992943) were identified close to *IMPAD1* (inositol monophosphatase domain containing 1) (Figure 1c). This gene encodes a member of the inositol monophosphatase family, which protein is localized to the Golgi apparatus and catalyzes the hydrolysis of phosphoadenosine phosphate to adenosine monophosphate. Openness was also associated with rs10876849 ($P=3.14\times10^{-6}$), near *OR10P1* (olfactory receptor, family 10, subfamily P, member 1) on chromosome 12q13.2. Olfactory receptors are responsible for recognizing and transducing G protein-mediated odorant signals. They interact with odorant molecules in the nose to initiate a neuronal response that triggers the perception of a smell.[48]

Regarding agreeableness, the most highly associated SNP (rs8015351, $P=1.27\times10^{-6}$) was located near *PRS29* (ribosomal protein S29), which contains a C2–C2 zinc finger-like domain that can bind to zinc (Figure 1d). Reactive zinc metal is crucial for neuronal signaling and is largely distributed within presynaptic vesicles, and further has an important role in synaptic function.[49] The protein encoded by this gene can enhance the tumor suppressor activity of Ras-related protein 1A. Two other SNPs in this gene region (rs7146832 and rs12880745) were also discovered to be associated with agreeableness.

Finally, both rs912765 and rs912764, located near *LMO4* (LIM domain only 4), were associated ($P=2.91\times10^{-6}$ and $P=7.36\times10^{-6}$, respectively) with conscientiousness (Figure 1e). This gene encodes a cysteine-rich protein, which may have a role as a transcriptional regulator. LMO4 is highly expressed in the hypothalamic nuclei that regulate glucose homeostasis with central insulin signaling.[50] Three SNPs (rs10471321, rs13178223 and rs7727166) located near *SFRS12* (also known as *SREK1*, splicing regulatory glutamine/lysine-rich protein 1) were also associated with conscientiousness. *SFRS12* encodes a member of a family of serine/arginine-rich splicing proteins containing RNA recognition motif domains, and there is the evidence that the cross-linking occurrence in neurons would be supported by detection of glutamyl-lysine in brain or cerebrospinal fluid.[51]

We expanded to top 100 SNPs because no SNPs were not replicated in the top five lists, and analyzed them in the Healthy Twin cohort (Supplementary Table 3). There were four SNPs (rs1189459, rs391792, rs7213162 and rs4726388) related to neuroticism, three SNPs (rs1460235, rs7840829 and rs2169164) related to conscientiousness, and seven SNPs (rs7030510, rs7858146, rs3739607, rs1029089, rs12521498, rs10814392 and rs3824425) related to agreeableness. Among the SNPs associated with agreeableness, rs1029089 were located near *PTPRD,* and the protein encoded by this gene is a member of the protein tyrosine phosphatase family known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle and oncogenic transformation.

Finally, we compared our results with them of the previous GWA and meta-analysis in Caucasian population.[1,27] The association between conscientiousness and *KATNAL2* was observed in this study ($P=0.038$, Supplementary Table 4).

DISCUSSION

To identify genetic variants associated with each of the five dimensions of personality, we performed a GWA meta-analysis of three cohorts participating a total of 3898 subjects. Though our results had no SNP reached the GWAS threshold, we found several new possible SNPs associated with personality traits. In other researches, however, the reported genes were only not consistent, but also the resulting genes were different and did not overlap between studies.[1,17,25–28,31] We found *TACC2* in neuroticism, *PTPN12* in extraversion, *IMPAD1* in openness, *RPS29* in agreeableness and *LMO4* in conscientiousness as the related genes of the first ranked SNPs. Among them, genes for neuroticism and conscientiousness were expressed in the brain, and the latter gene had evidences about the association with neuropsychiatric conditions like schizophrenia or Alzheimer's diseases.[52,53] *PRS29* containing a zinc finger-like domain was identified in agreeableness, and the variant of the gene encoding Zinc Finger Protein 804A was known as one of the strongest risk factors of schizophrenia and schizotypal personality traits.[54,55] Besides the highest associated SNPs, *PLXDC2,* the gene associated with plexins, which function as receptors for the repulsive axonal guidance molecules semaphorins, was found in neuroticism.[56] Axon guidance was known as a key stage in the formation of neuronal network, and a recent GWAS identified that a variant of the gene encoding plexin A2 was associated with anxiety, depression, neuroticism and psychological distress.[57] Among the top five SNPs in extraversion, *KIRREL3* was also expressed in the brain and reported to associate with autism or Jacobsen syndrome.[58,59] *OR10P1* was discovered in openness, and the association between personality and olfactory receptors has also been explained in another report.[60,61] These relations could be helpful to further understanding on effects of personality traits and olfactory functioning for psychiatric diseases like panic disorder.[62] Therefore, these results support the hypothesis that the genes could affect to neuropsychiatric phenotypes as well as personality traits.

Furthermore, we expanded the investigation to top 100 SNPs because no SNPs of top five were replicated in Healthy Twin cohort. In top 100 lists, a SNP encoded to *PTPRD* in agreeableness, which had reports on association with other personality trait.[9,31] The *PTPRD* was modestly associated with Persistence in Cloninger's Temperament and was found moderate association signals for openness in our previous study, even though failed to replicate. This gene was also reported that this gene was associated with ADHD and obsessive–compulsive disorder.[63,64] Comparing with previous results of Caucasian population[1,27] we confirmed the association between conscientiousness and the SNP located in an intron of *KATNAL2*. This gene is widely expressed in the central nervous system and encodes a protein similar to the A subunit of the p60 katanin protein, which acts to sever microtubules in the axons of neurons. It is thought to have a role in neurodevelopment owing to neuronal migration, axonal growth and dendritic pruning.[65–68] Meta-analysis on GWAS is an increasingly popular tool for combining multiple studies in a single analysis to identify associations with small effects,[69,70] but there was a problem that the reported genes from several GWAS on personality genomics were not consistent.[25–28] Therefore, our study could be noteworthy to confirm some SNPs of previous results.

In this study, however, we found that some results were not consistent with our previous study, even though populations of previous study were included in current meta-analysis. In our previous report, several SNPs close to olfactory receptor 1A2 (*OR1A2*) were replicated, but rs12601685-encoded *OR1A2* were not identified in current study. The reason might be the different reference platform for imputation, that is, rs12601685 was one of the SNPs imputed from previous reference platform, which could not be included in this study. Moreover, *PTPRD* was associated with agreeableness in current study, whereas its association was reported in openness in our previous study.[9] We supposed that the reason might be correlation between personality traits. Theoretically, the five factors of personality are orthogonal, but recent studies have found that the five factors are actually substantially inter-correlated.[8,71]

In conclusion, this study is meaningful as it was the first GWA meta-analysis on a non-Caucasian population, especially East-Asian, targeted to FFM personality traits. There were several SNPs associated with personality, and we also confirmed some SNPs of own and previous results. The findings of our GWA meta-analysis suggest that the genes related to personality traits could be susceptible to neuropsychiatric phenotypes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

The genotype data were gratefully made available by the Center for Genome Science, Korea National Institute of Health, Korea Centers for Disease Control and Prevention. This research was supported by the National Research Foundation of Korea (NRF), funded by the Ministry of Education (NRF-2010-0026606, NRF-2013R1A1A2062702) and Ministry of Science, ICT & Future Planning (NRF-2014R1A2A2A04006291), and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare, Republic of Korea (HI14C0072).

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Supplementary Information accompanies the paper on Journal of Human Genetics website (http://www.nature.com/jhg)