Chauhan *et al.*
Egyptian Journal of Medical Human Genetics (2022) 23:57
https://doi.org/10.1186/s43042-022-00266-0

Egyptian Journal of Medical Human Genetics

REVIEW

Open Access

Cataloging the potential SNPs (single nucleotide polymorphisms) associated with quantitative traits, viz. BMI (body mass index), IQ (intelligence quotient) and BP (blood pressure): an updated review

Waseem Chauhan, Rafat Fatma, Afiya Wahab and Mohammad Afzal*

Abstract

Background: Single nucleotide polymorphism (SNP) variants are abundant, persistent and widely distributed across the genome and are frequently linked to the development of genetic diseases. Identifying SNPs that underpin complex diseases can aid scientists in the discovery of disease-related genes by allowing for early detection, effective medication and eventually disease prevention.

Main body: Various SNP or polymorphism-based studies were used to categorize different SNPs potentially related to three quantitative traits: body mass index (BMI), intelligence quotient (IQ) and blood pressure, and then uncovered common SNPs for these three traits. We employed SNPedia, RefSNP Report, GWAS Catalog, Gene Cards (Data Bases), PubMed and Google Scholar search engines to find relevant material on SNPs associated with three quantitative traits. As a result, we detected three common SNPs for all three quantitative traits in global populations: SNP rs6265 of the BDNF gene on chromosome 11p14.1, SNP rs131070325 of the SL39A8 gene on chromosome 4p24 and SNP rs4680 of the COMT gene on chromosome 22q11.21.

Conclusion: In our review, we focused on the prevalent SNPs and gene expression activities that influence these three quantitative traits. These SNPs have been used to detect and map complex, common illnesses in communities for homogeneity testing and pharmacogenetic studies. High blood pressure, diabetes and heart disease, as well as BMI, schizophrenia and IQ, can all be predicted using common SNPs. Finally, the results of our work can be used to find common SNPs and genes that regulate these three quantitative features across the genome.

Keywords: SNPs, Polymorphisms, Quantitative traits, dbSNP, SNPedia, BMI, IQ, BP

Background

In the presence of an environmental stimulus, genetic differences arise within and between populations, resulting in polymorphisms that can be connected to a hereditary trait or phenotype. SNPs (pronounced "snips"), or single nucleotide polymorphisms, are the most frequent type of DNA sequence variation detected in people. Each SNP refers to a change in a single nucleotide, which is a DNA building unit. SNPs occur naturally in everyone's DNA and are found around every 300–2000 base pairs across the genome [1]. On average, there are 84.7 million single nucleotide polymorphisms (SNPs) in the human genome [2], including both coding and non-coding regions of the genes. SNPs can be used as biological

*Correspondence: ma.afzal1235@gmail.com; afzal1235@rediffmail.com
Human Genetics and Toxicology Laboratory, Section of Genetics, Department of Zoology, Aligarh Muslim University, Aligarh 202002, India

markers to assist researchers in finding out genes linked to disease. Regulatory SNPs are oligonucleotide substitutions that occur in regulatory regions and control gene expression. SNPs found within a gene or in a regulatory region around a gene may thus have a direct effect on the condition by altering the gene's function. In general, these SNPs are linked to complex traits, which can represent unique characteristics of an organism or an individual [1, 3]. Moreover, genes, environment and their interactions can influence these traits. Genetically, all traits are divided into two categories based on their effect on an organism's phenotype, i.e., qualitative and quantitative. Quantitative traits (QTs aka complex traits) are phenotypic traits that are determined by a large number of small-effect genes in combination with the environment, e.g., crop yield, plant disease resistance, diabetes, skin color, weight gain in animals, body mass index (BMI), intelligent quotient (IQ), learning ability, blood pressure (BP), etc. QTs can also be categorized into three different ways: (I) morphometric traits cover the analysis of morphology or size and shape of any individual, e.g., BMI; (II) psychometric traits measure the cognitive ability and mental agility of a person, e.g., IQ; and (III) physiometric traits related to the physiological measurements of the body, e.g., BP. In this article, we emphasize three QTs mentioned above. BMI is a mathematical approach used to estimate a person's health status based on height and weight (BMI = weight (kg)/(height (m^2)). BMI helps us to categorize the person's health into four groups, i.e., underweight (BMI below 18.5), normal or healthy weight (18.5–24.9), overweight (25.0–29.9) and obese (30) and above [4]. IQ refers to the efficacy of mental functioning underlying behavior depending on specific criteria. Therefore, it is used to see how effectively someone can utilize reasoning and facts to answer questions and make predictions. The equation used to calculate a person's IQ score is $\frac{\text{mental age}}{\text{chronological age} \times 100}$. Home-Global IQ Institute. Factors influencing IQ are genetics, genotype–environmental (GXE) interaction, gender, family and school environment, society influence (poverty/race/ethnicity), etc. [5]. Another trait is BP, which is expressed as a two-digit figure, i.e., SBP and DBP (systolic and diastolic blood pressure). Hypertension is defined as an increase in BP of greater than 140/90 mmHg. In contrast, hypotension is defined as a SBP of 90/60 mmHg or lower. BP is a complex condition, and various factors, including heredity, physiology, environmental reaction, lifestyle, etc., influence it [6, 7]. Although these quantitative traits have been extensively studied, various studies have reported phenotypic associations among all three traits; therefore, a common SNP-based study of the association becomes essential [8–15]. To our knowledge, no common SNPs or polymorphisms have been categorized concerning these three quantitative variables, namely BMI, IQ and BP. So, in the present study, we searched and tabulated various SNPs related to these attributes. SNPedia, RefSNP Report, GWAS Catalog, Gene Cards (Databases), PubMed and Google Scholar search engines were used to find relevant information about SNPs related to three QTs, using the keywords "Quantitative traits SNPs", "BMI SNPs", "IQ SNPs", "hypertension/hypotension SNPs", "role of SNPs", "Gene function", and "GWAS" in various combinations. More than 340 articles were retained by using the aforementioned keywords, and about 182 pieces of literature (reviews and original articles) stating significant associations were included. Then, all SNPs were tabulated related to traits in question, and finally common SNPs were uncovered for the same.

SNPs associated with BMI

Various genome-wide association studies (GWAS) and extensive population-based research have discovered many SNPs linked to BMI/obesity. SNP such as rs653178 (12q24.12) is present in the intron of the gene ATXN2 (Ataxin-2), which codes proteins that are required essentially for endocytosis and mitochondrial functions ($p < 5 \times 10^{-7}$). GWAS and other knock-out studies have shown that ATXN2 regulates Ca^{+2} storage and enzymes of mitochondrial matrix and may develop insulin resistance and dyslipidemia after loss of its functions and ultimately leads to high BMI/Obesity [13–16]. Another SNP rs12411886 is also present in the intronic region of gene CNNM2 on chromosome 10; a GWAS has reported its association ($p < 4 \times 10^{-5}$) with BMI and cardiovascular risk disease (CVD). However, CNNM2 called cyclin M2 encodes for transmembrane protein involved in the transport of Mg^{+2} ions and is highly expressed during brain and kidney development. rs794356 is present in the intron of HIP1 (7q11.23) gene. HIP1 (huntingtin-interacting protein-1) encodes for a protein, i.e., one of the members of clathrin mediated endocytosis and trafficking; therefore, HIP1 is necessary for fundamental cellular and organismal homeostasis in vivo phenotypes and deficiency of HIP1 may lead to adult weight loss and early death [17]. rs1167266 is another SNP associated with BMI located in the intronic sequence of GIPR gene on chromosome 19 ($p < 1.64 \times 10^{-4}$). This gene encodes a G-protein coupled receptor for gastric inhibitory polypeptide (GIP), which was first discovered in gut extracts to block stomach acid production and gastrin release but was later shown to promote insulin release in context of high glucose. According to knock-out research on $GIPR^{-/-}$ mice, an oral glucose dosage raises blood glucose levels with compromised early insulin response; as a result, a mutation in this gene may have a role in development of diabetes [18]. Another trans-ethnic

analysis of metabochip data has identified two SNPs rs2820436 ($p < 3.79 \times 10^{-8}$), LYPLAL1 on chromosome 1 and rs10930502 ($p < 2.5 \times 10^{-7}$) METAP1D on chromosome 2 associated with BMI. The LYPLAL1 (Lysophospholipase Like 1) gene codes for a protein that plays a role in hydrolase activity and lysophospholipase activity, while METAP1D (Methionyl Aminopeptidase Type 1D) is a mitochondrial protein coding gene that is associated with aminopeptidase activity and metalloaminopeptidase activity; thus, these activities might have possible impact on pathways that regulate metabolism and adipose tissue [19]. Some other SNPs like rs1934100 ($p < 5 \times 10^{-8}$) in ELAVL2 gene on chromosome 9 and rs1720825 in MRAS gene on chromosome 3 are also intron variants, while rs754635 ($p < 5 \times 10^{-8}$) in CCK gene on chromosome 3 is splice region variant, and rs7176527 in ZSCAN2 on chromosome 15 is intergenic variant. All these SNPs are linked to an increase in BMI [17, 19–21], while rs1720825, rs7176527, rs1167266, rs794356 and rs653178 are linked to additional traits, e.g., CVD, waist circumference (WC), type II diabetes (T2D), glucose homeostasis, insomnia and DBP, respectively [17]. There is a list of SNPs associated with BMI (Table 1).

SNPs associated with IQ

Since intelligence is associated with important economic and health-related life outcomes, a genome-wide association meta-analysis of 78,308 individuals identifies 336 SNPs associated with intelligence, implying that genes are important in regulating the maturation of neurons and others linked to intellectual disability and cerebral malformation [67]. Apart from rs12411886 in CNNM2 (mentioned above), there are various other SNPs like rs66495454 in NEGR1, ($p < 9.08 \times 10^{-9}$), rs236330 in FNBP1L and rs12744310 ($p < 4.2 \times 10^{-9}$) chromosome 1; rs3846329 in NR3C2 at chromosome 4; rs2490272 in FOXO3 and rs1011313 in DTNBP1 gene at chromosome 6; rs10236197 in PDE1C ($p < 1.03 \times 10^{-10}$) at chromosome 7; rs411280 in NTM at chromosome 11; rs2251499 intergenic at chromosome13; rs16954078 in SKAP1($p < 2.84 \times 10^{-8}$) at chromosome 17; and rs113315451 in CSE1L ($p < 1.15 \times 10^{-8}$) at chromosome 20 are linked to IQ [68–71]. NEGR1 codes for neuronal growth regulators and is associated with Niemann–Pick disease and leptin deficiency/dysfunction. It is involved in cell adhesion and functions as a trans-neural growth-promoting factor in regenerative axon sprouting in the mammalian brain (genecard.org). While another gene on chromosome 1 encoding a protein that promotes CDC42-induced actin polymerization by activating the N-WASP-WIP complex, FNBP1L produces a protein that promotes CDC42-induced actin polymerization by activating the N-WASP-WIP complex. Actin polymerization may increase membrane tubule fission and the formation of endocytic vesicles. rs2490272 is an intronic FOXO3 (Forkhead Box O3) SNP that was found to be associated ($p < 9.96 \times 10^{-14}$) with intelligence. FOXO3 is a gene that codes for proteins which activate PI3K/AKT and cause apoptosis in the absence of survival factors, including neuronal cell death in response to oxidative stress. Details of additional IQ-related SNPs (Table 2).

SNPs associated with BP (hypertension / hypotension)

A number of SNPs were identified with a varied impact on BP. Some SNPs that are identified in strong association with BP. A GWAS of blood pressure based on 200,000 European peoples has identified 16 new loci it. Out of these loci, the rs11953630 ($p = 1 \times 10^{-4}$) is found in EBF1 gene at chromosome 5, coding for EBF transcription factor 1, a DNA binding homodimer that forms complexes with the Mb1 promoter, and strongly activates the transcription. Some studies have found high levels of Ebf expression in lymph node, spleen, and adipose tissues and low levels in several nonlymphoid tissues [65, 97], Another BP-associated variant rs7129220 ($p = 4 \times 10^{-7}$) is an intronic variant present in AMPD3 at chromosomes 11(11p15.4). This gene is responsible for coding Adenosine Monophosphate Deaminase 3, an enzyme involved in adenylate catabolic pathway, in which it converts adenosine monophosphate to inosine monophosphate, by hydrolytic deamination process; therefore, it has critical role in energy metabolism and vascular blood flow to direct nutrient and oxygen delivery (www.omim.org; www.genecards.org; [65]. The rs805303 is considerably associated with hypertension ($p = 1 \times 10^{-10}$) and found in BAG6 at chromosome 6 [65, 98]. The BAG6/BAT3 complex functions as a chaperone, preventing soluble proteins from aggregating and assisting in their transport to the endoplasmic reticulum or, alternatively, promoting their sorting to the proteasome, where they are degraded. As a result, the BAG6 protein is engaged in a variety of cellular activities, including apoptosis, gene regulation, protein synthesis, quality management and protein degradation. It is yet unclear if the variation rs805303 affects BAG6's regulatory or functional capabilities. According to expression analyses, the 'AA' genotype of rs805303 reduces BAG6 expression in the coronary and tibial arteries, the aorta, the sigmoid colon and the esophagus www.genecards.org [99]. The rs2286672 ($p = 3 \times 10^{-9}$) in PLD2 locus at chromosome 17 is a missense variant (R172C) and found associated with hypertension. Although PLD2 gene encodes for phospholipase 2 protein and essentially acts in the hydrolysis of phosphatidylcholine to phosphatidic acid and choline, PLD2 is also involved in cytoskeletal organization, cell cycle control,

Table 1 SNPs related to BMI, chromosomal location, name of gene, allele, effect of that SNP and other associated traits

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs2229616	18q21.3	MC4R	C > T	Decreased glycosylated hemoglobin, increased HDL cholesterol	0.020	Decreased waist circumference, decreased blood sugar levels, increased in good cholesterol levels	7888		[22]
rs1121980	16q12.2	FTO	G > A G > C	Increasing BMI	1.13×10^{-7}	WC	20,374		[23, 24]
rs17782313	18	MC4R	T > A T > C	High BMI	< 0.05	BP, T2D	216		[25–27]
rs7359397	16p11.2	SH2B1	C > A C > T	Increased BMI	1.88×10^{-20}	Schizophrenia intelligence, self-reported education attainment	249,796	GWAS	[26]
rs13107325	4p24	SLC39A8	C > A C > T	Increased BMI	1.50×10^{-13}	BP	249,796	GWAS	[26]
rs5443	12p13	GNB3	C > T	Enhanced G-protein activation	0.00002	Obesity, diabetes		Candidate	[28]
rs10767664	11p14.1	BDNF	T > A T > G	neuronal regulators of appetite or energy balance, increased BMI	4.69×10^{-26}	Coronary artery disease (CAD), allergy/asthma	249,796	GWAS	[26]
rs174575	11q12.2	FADS2	C > G		0.018		1037		[29]
rs5068	1p36.22	NPPA	A > G, T	Low BP	4×10^{-5}	BMI, metabolic syndrome		Candidate	[30, 31]
rs1535	11q12.2	FADS2	A > G A > T	Decline ability to elongate and desaturate fatty acid		BMI	1037		[29, 32]
rs17700633	18q21.3	MC4R	G > A	increased BMI	0.01	T2D	14,940		[33]
rs1299548	7p21.3	Near C1GALT1	G > A G > C	Visceral adipose tissue, BMI	0.039	VAT	2513	GWAS	[34]
rs12517906	5q35.3	LOC1002899003/MGAT1	C > A C > T	Fat absorption	$7.3 \times 10^{-8}/6 \times 10^{-6}$	Weight	7373	GWAS	[35]
rs7759938	6q16.3	LIN28B	C > A C > G C > T	Sex-specific height-growth-regulating effects	5×10^{-11}	Influencing age at menarche/epithelial ovarian cancer	8903	GWAS	[36]
rs9939609	16q12.2	FTO	T > A	Increasing BMI	2×10^{-7}	T2D obesity, high BP	38,759	GWAS	[37]
rs4285184	5q35.3	MGAT1	A > G	Affect the levels of serum unsaturated fatty acid	0.001	Obesity	1152/1076/2249	GWAS	[38]
rs1021001	5q35.3	MGAT1	C > G	Affect the level of serum unsaturated fatty acid	0.003	Obesity	1152/1076/2249	GWAS	[38]

Table 1 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs939584	2p25.3	TMEM18	C > G C > T	BMI at 20 years	2.03×10^{-5}		11,586	GWAS	[39]
rs662799	11q23.3	APOA5	G > A G > C	Higher fasting triglyceride levels	2×10^{-71}	HDL cholesterol, myocardial infarction	2280		[40]
rs13021737	2p25.3	TMEM18	A > C A > G A > T	Increased BMI	0.018	Obesity	17,037		[41]
rs1558902	16q12.2	FTO	T > A	Maximum BMI	0.037	T2D, WC, obesity	1450		[42]
rs11030100	11p14.1	BDNF	G > A G > T		1×10^{-28}	Postpartum depression	173,430	GWAS	[39]
rs1421085	16q12.2	FTO	T > C	Decreased mitochondrial energy generation and increased triglyceride accumulation	6×10^{-39}	T2D			[43]
rs11191580	10q24.33	NT5C2	T > C	Increased BMI	3.83×10^{-8}	Schizophrenia bipolar disorder major depression	86,757/7488–47,354		[44]
rs2535633	3p21.1	ITIH4ITIH4-AS1			1.77×10^{-10}		86,757/7488–47,354		[44]
rs8050136	16q12.2	FTO	C > A	Increased BMI	4×10^{-8}	T2D	4189		[45]
rs12374818	7p	Near BBS9 and VAT			1.1×10^{-7}		2513	GWAS	[34]
rs3751812	16q12.2	FTO	G > T	Increased BMI	6×10^{-108}			GWAS	[46]
rs17817449	16q12.2	FTO	T > A, T > G	Increased BMI	6×10^{-108}			GWAS	[21, 46]
rs10506943	12	CYCSP30 and VAT-BMI	T > C	VAT-BMI	2.42×10^{-7}		2513		[34]
rs12186500	5q35.3	MGAT1	A > G	Ý-Linolenic acid, arachidonic acid, delta 6 and 9 desaturase	0.017		1152/1076/2249	GWAS	[38]
rs143665886	7q31.2	LINC01392	T > C		< 0.0001	Diabetes hypertension	3922	GWAS	[47]
rs11642015	16q12.2	FTO	C > T	High BMI	0.001	Diabetes obesity	1536	GWAS	[48]
rs11583200	1p33	ELAVL4	C > T	Effect positive direction with BMI	0.008		17,037		[41]
rs16858082	4p12	GNPDA2		Leptin level elevate	3×10^{-4}	WC, percent body fat and upper arm circumference	3506	GWAS	[49]
rs12229654	12q24.11	CUX2	T > G		4.56×10^{-9}	Myocardial infarction, high-density lipoprotein cholesterol levels	86,757/7488–47,352		[44]

Table 1 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs2383207	9p21.3	CDKN2B-AS1	A/G	Increased fasting glucose level	0.001	Weight gain	350	RT-PCR	[50]
rs10146997	14q31.1	NRXN3	A > G		0.0028	T2D WC	7225		[51]
rs261967	5q15	Near PCSK1	A > C	Deregulation lipid metabolism Pancreatic dysfunction	8×10^{-13}	Obesity T2D appendicular lean mass	2215	GWAS	[52]
rs4776970	15q23	MAP2K5	A > C A > G A > T		3×10^{-7}	WC, T2D, depressive disorder, schizophrenia, bipolar disorder	1624		[53]
rs10913469	1q25.2	CRYZL2P-SEC16B	T > C		0.0041	WC	7225	GWAS	[51]
rs10938397	4p12	GNPDA2	A > G	increased BMI	0.00093	DBP, WC, waist-to-height ratio and fat mass percentage	3077/3,503	GWAS	[54]
rs6548238	2p25.3	TMEM18	T > C/T > G	Increased BMI	1×10^{-18}		45,069		[55]
rs12597579	16p12.3	SNRPEP3	C/A/T		1×10^{-8}		2813	TaqMan 5′exonuclease allelic discrimination assay	[56]
rs11142387	9q21.12	KLF9	A > T A > C	Higher BMI	3.4×10^{-4}	Psychiatric disease, memory, performance	62,245/1624	GWAS	[57]
rs13130484	4p12	GNPDA2	C > T C > A	Higher BMI	3.4×10^{-4}		8914		[58]
rs4680	22q11.21	COMT	G > A	Transfers methyl group to catecholamines, to inactivate	< 0.01	Weight gain/ decreased SBP	165/6969		[59–61]
rs2206734	6p22.3	CDKAL1	C > G/C > T	Decreasing BMI	1.4×10^{-11}	T2D	62,245	GWAS	[57]
rs7138803	12q13.12	FAIM2	G > T/G > A	Increased BMI	0.015	WC, obesity. DBP	3077/249796		[54, 62]
rs987237	6p12.3	TFAP2B	A > G	Increased BMI	$< 5 \times 10^{-8}$	Obesity	249,796	GWAS	[62]
rs2241423	15q23	MAP2K5	G > A	Increased BMI	0.029	obesity	474/519/2308	TaqMan polymorphism assay	[63]
rs206936	6p21.31	NUDT3	A > G	Increased BMI	5.3×10^{-5}		1424	GWAS	[64]
rs1514175	1p31.1	TNNI3K	C > T	Increased BMI	5.54×10^{-5}		7225		[51]
rs653178	12	ATXN2	C > G C > T	High BMI	5×10^{-7}	DBP		GWAS	[56]
rs12411886	10q24.32	CNNM2Intron variant	C/A	High BMI	4×10^{5}	CAD		GWAS	[17]
rs198358	1p36.22	NPPA-A1	T > C	BMI hypotension	2×10^{-4}	Hypotension	1507	Candidate	[65, 31]
rs794356	7	HIP1	G > A	High BMI	1×10^{-5}	Insomnia			[17]

Table 1 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs11672660	19q13.32	GIPR	C > T	High BMI	1.64×10^{-4}	T2D, glucose homeostasis			[20]
rs2820436	1q41	LYPLAL1	A/C	High BMI	$< 3.79 \times 10^{-8}$		102,514	PAGE	[19]
rs10930502	2q31.1	METAP1D	A/G	High BMI	$< 2.5 \times 10^{-7}$		102,514	PAGE	[19]
rs1934100	9p21.3	ELAVL2	A/T	High BMI	$< 5 \times 10^{-8}$		200,452	GWAS	[19]
rs754635	3p22.1	CCK	G/C	High BMI	$< 5 \times 10^{-8}$		200,452	GWAS	[19]
rs7176527	15q25.2	ZSCAN2	C/T	BMI-adjusted WC	$< 5 \times 10^{-8}$	WC	200,452	GWAS	[19]
rs1720825	3q22.3	MRAS	A/G		4×10^{-6}	CAD	200,452		[19]
rs671	12q24.12	ALDH2	G > A	Increased BMI	3.4×10^{-11}	Hypertension	757/7488–47,352.4204–5435	GWAS	[44, 66]
rs4771122	13q12.2	MTIF3	G > A G > C G > T	Increased BMI	$< 5 \times 10^{-8}$	Obesity	249,796		[62]
rs6265	11p14.1	BNDF	C > T		1×10^{-14}	Obesity hypertension short-term plasticity and learning	3503	GWAS	[39]

Table 2 SNPs related to IQ, chromosomal location, gene, allele, effect of that SNP and other associated traits

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs324650	7q33	CHRM2	T > A		PIQ-6.0 VIQ-1.8 FSIQ-4.0	Alcohol dependence and major depression	667		[72]
rs10457441	6q16.1	MIR2113	T > A T > C T > G	Decline in episodic memory	< 0.02		1570	GWAS	[73]
rs17522122	14q12	AKAP6	G > T	Worse performance in episodic memory Working memory Vocabulary and perceptual speed	4×10^{-9}		1570	GWAS	[73]
rs363039	20p12.2	SNAP25	G > A G > C G > T	Highly associated with IQ variations	< 0.01		762		[72]
rs2721173	8q24.3	LRRC14	C > T		9×10^{-6}		106,736/24,189		[74]
rs11584700	1q32.1	Near gene LRRN2	A/G		2.1×10^{-9}		101,069	GWAS	[74]
rs7923609	10q21.3	JMJD1C, MIR1296	A > G		1×10^{-6}		106,736/24,189		[74]
rs4851266	2q11.2	AFF3, LINC01104	C > T		5×10^{-11}		26 population	GWAS	[75]
rs17518584	3p12.1	CADM2	C > T C > A	Processing speed	0.013	T2D	944	GWAS	[76]
rs1487441	6q16.1	LOC101927335 AL589740.1	G > A		2×10^{-9}		106,736/24,189		[74]
rs3213207	6	DTNBP1	A/G		0.109			Single base primer extension	[77]
rs2350780	7q33	CHRM2	G > A	Involved in neuronal excitability, synaptic plasticity and feedback regulation of acetylcholine release and performance IQ (PIQ)	0.016		371, 391		[78]
rs35753505	8p12	NRG1	T > A T > C T > G	Increased performance in cognitive domains and IQ			218		[79]
rs821616	1q42.2	DISC1	A > T			Schizophrenia and bipolar disorder	425		[80]
rs1800497	11q23.2	ANKK1	G > A	Insight problem solving	0.033		425		[81]
rs174575	11q12.2	FADS2	C > G		0.018		1037		[29]

Table 2 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs1535	11q12.2	FADS2	A > G A > T	Decline ability to elongate and desaturate fatty acid		BMI	1037		[29, 32]
rs17070145	5q34	WWC1	C > G/C > T	Associated with episodic memory performance	0.001	Alzheimer's disease	N = 8909, N = 4696		[82]
rs6439886	3q23	CLSTN2	A > G	Increased memory performance		Alzheimer's disease cognitive impairment		GWAS	[83]
rs363043	20p12	SNAP-25	C > T	Increased IQ	< 0.01		Children-371 Adult-391		[84]
rs363016	20p12	SNAP-25	C > T	Increased IQ	0.0001		Children-371 Adult-391		[84]
rs6265	11p14.1	BDNF, BDNF-AS	C > T	short-termlearning		Obesity Hypertension		GWAS	[85]
rs2619539	6p22.3	DTNBP1	C > A C > G			Schizophrenia	235		[86]
rs362602	20p12-p11.2	SNAP-25	A > G	Increased verbal IQ (VIQ)	0.005		232 793		[87]
rs3758391	10q21.3	SIRT1	T > C			Cardiovascular disease diabetes	682, 563		[88]
rs11809911	1q23.3	LMXA1		Associated with reduced IQ and memory/learning			218		[79]
rs9320913	6q16.1	LOCI100129158 AL589740.1	C > A		4.2×10^{-9}		101,069	GWAS	[89]
rs6948054	7q31-35	CHRM2	A > G A > C	PIQ	0.041		2158		[78]
rs8191992	7q31-35	CHRM2	A > T		0.036		2158		[78]
rs2619528	6	DTNBP1	C > T	Logical memory immediate Symbol search Random letters decrease performance	0.098		1054, 1806, 745		[77]
rs760761	6p22.3	DTNBP1	G > A	VIQ, full scale IQ (FSIQ)	0.026		108		[77]
rs324640	7q31-35	CHRM2	G > A G > T		PIQ-5.2 VIQ-1.2 FSIQ-2.9		667		[72]

Table 2 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs2619522	6	DTNBP1	A > C	Minor allele-lower cognitive ability	< 0.01	Schizophrenia	7,592		[90]
rs2061174	7q31-35	CHRM2	G > C G > A	Strongly associated with intelligence	< 0.01		371/391		[91]
rs17800861	16p13.2	GRIN2A	T > A		2.98×10^{-7}		2,421		[92]
rs10119	19q13.32	TOMM40	G > A	Associated with general fluid cognitive function	5.67×10^{-9}		539,490		[93]
rs4680	22q11.21	COMT	G > A	Transfers methyl group to catecholamine, to inactivate	< 0.01	Weight gain/ decreased SBP	165/6969		[59–61]
rs4962322	10q26.2	ADAM12	C > A C > G C > T	Gene family PLEXIN member are mutated	8×10^{-9}		1238	GWAS	[94]
rs10794073	10q26.2	ADAM12	A > C A > G A > T		2.02×10^{-8}		1238	GWAS	[94]
rs1799990	20p13	PRNP	A > G	Associated with a decrease in spatial span, letter number sequencing and matrix reasoning scores	≤ 0.05		1091		[95]
rs1276529	6q21	RFPL4B	G/A/C/T	VIQ	1×10^{-6}		2421	GWAS	[92]
rs1706066	6	RFPL4B		VIQ	7.13×10^{-7}		2421	GWAS	[92]
rs1276583	6	RFPL4B		VIQ	1.42×10^{-6}		2421	GWAS	[92]
rs12552228	9	TEK		Functional IQ(FIQ)/PIQ	8.51×10^{-7}/PIQ-3.8×10^{-6}		2421	GWAS	[92]
rs12554799	9	TEK		FIQ/PIQ	8.51×10^{-7}/PIQ-3.8×10^{-6}		2421	GWAS	[92]
rs705670	9q34.3	LINCO1502	C > G C > T	PIQ	3.09×10^{-7}		2421	GWAS	[92]
rs4962520	10q26.2	ADAM12	C > T		1.2×10^{-8}		1238	GWAS	[94]
rs2490272	6q21	FOX 03	C/A/G/T	Positive effect	9.96×10^{-14}	Associated with human longevity	78,307	GWAS	[69]
rs10236197	7p14.3	PDE1C	T/A/C/G	Showed positive effect	1.03×10^{-10}		78,307	GWAS	[69]
rs2251499	13q33.2	intergenic	T/A/C/G	Showed positive effect	2.74×10^{-10}		78,307	GWAS	[69]

Table 2 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample	Method/study	References
rs66495454	1p31.1	NEGR1	TCC/TCCT		9.08×10^{-9}	Diet measurement	54,119	GWAS	[69]
rs113315451	20q13.13	CSE1L Intron variant			1.15×10^{-8}		54,119	GWAS	[69]
rs236330	1	FNBP1L	C > T	Associated with IQ in adult and children	3.9×10^{-15}		17 989		[68]
rs1011313	6	DTNBP1	T > A/ T > C	Working memory, executive function, freedom from distractibility	< 0.05		1054 Scottish, 1806 Australian and 745 English		[70]
rs16954078	17q21.32	SKAP1 Intron variant	T/A	Negative effect on IQ	2.84×10^{-8}		65,866	GWAS	[69]
rs411280	11q25	NTM	T > A T > C	FSIQ	$< 10^{-3}$		292 nuclear family	GWAS	[71]
rs3846329	4q31.23	NR3C2	G > C G > T	FSIQ	$< 10^{-3}$		292 nuclear family	GWAS	[71]
rs363050	20p12.2	SNAP25	G > A	VIQ	< 0.01		Children-371 Adult-391		[84]
rs13107325	4q24	SLC39A8	C > A C > T	High blood Mn causes lower performance for certain IQ subtests, increased sway and increased scores for behavioral problems	< 0.001		686		[96]

transcriptional regulation and/or regulated secretion. Another missense variant, rs16835244 ($p = 1 \times 10^{-3}$), is found on chromosome 1 in AZIN2 and substitutes Ala288 in the arginine decarboxylase (ADC) with serine [98]. Antizyme inhibitor (AZIN) family member arginine decarboxylase (ADC) assist in cell growth and proliferation by ensuring polyamine homeostasis inside the cell [100]. rs4963 and rs17833172 in ADD1 at chromosome 4 have been strongly associated to the BP. A study looked at the relationship between the rs17833172 variation and systolic, diastolic and mean arterial pressure in responses to a high-sodium intervention, as well as DBP responses to a low-sodium intervention. Two copies of the 'A' allele of rs17833172 reduce the response to salt consumption substantially [101]. Similarly, another study found rs4963, which is Gly460Trp polymorphism of ADD1 gene, to be involved ($p = 0.0003$) in the increased salt sensitivity of BP and hypertension [101–103]. The gene NEDD4L, which controls the amiloride-sensitive epithelial sodium channel, is also a potential gene for salt sensitivity (ENaC). In NEDD4L at chromosome 18, rs2288774 (C/T) polymorphism and rs4149601 (G/A), GG genotype is essential for encoding the protein's C2 domain. These NEDD4L genotypes were shown to be therapeutically beneficial ($p = 0.007$ and $p = 0.07$) in identifying patients, who benefit from dietary salt restriction in management of hypertension [102, 103]. A study during the Japanese National Project shows two SNPs rs3794260 (G/A) ($p = 0.0001$) and rs9739493 (T/C) in KIAA0789 at chromosome 12, exhibited the susceptibility of KIAA0789 gene for hypertension [104]. Another study analyzed 14 million variants among 815 adolescents for genetic association studies of BP showed the association of rs181430167 ($p = 6.8 \times 10^{-7}$) with SBP and rs12991132 ($p = 4.0 \times 10^{-7}$) with DBP [105]. For additional SNPs concerning BP, see Table 3. After tabulating all the collected data of SNPs, we arranged these different SNPs according to their involvement in the determination of any two or three traits.

Common SNPs associated with BMI and BP/hyper-hypotension

We discovered some SNPs that are actively participating in determination of BMI and BP [132]. Scientists examined through study of ~15,000 Europeans that the rs5068 in NPPA gene is (3′UTR region variant) at 1p36.22 chromosome, is strongly associated ($p = 8 \times 10^{-70}$) with increased circulating natriuretic peptide and thus lower BP. The gene CDKN2B-AS1 produces a functional RNA molecule that interacts with polycomb repressive complexes 1 and 2, resulting in epigenetic silencing of other genes in the cluster. This region is also linked to a variety of different diseases, including numerous malignancies, intracranial aneurysms, T2D, periodontitis, Alzheimer's disease, endometriosis, weakness in the elderly and glaucoma. The SNP rs2383207 in CDKN2B-AS1(Intron variant) found at chromosome 9 (9p21.3) was proposed to be linked with elevated risk for coronary artery disease in a Korean population ($p = 0.001$) [139], ischemic stroke risk in Sweden people ($p = 0.04$) [140] and G allele of SNP rs2383207 with the internal carotid artery and intima-media thickness ($p = 0.007$) [141] therefore, such genetic variation at the CDKN2A/CDKN2B locus can be used as a marker to predict stroke in hypertensive patients [131]. Some other reports have found that obesity, BMI, coronary artery disease (CAD), insulin resistance and therefore diabetes, left ventricular hypertrophy and hypertension have all been related to rs5443 in the G-protein beta3 subunit (GNB3) gene at 12p13 chromosome, which is more generally known as the C825T variation [28, 142]. Another gene, named FTO (FTO Alpha-Ketoglutarate Dependent Dioxygenase) also known as "Fat gene", has rs9939609, an intron variant at 16q12.2 chromosome, which is related to SBP [54] elevated BMI along with rs17782313 on MCAR (Intergenic variant) at 18q21.3 [143] and negatively associated with DBP and mean BP with hypertension [25]. The rs10938397 on GNPDA2 (Intergenic variant) at 4p12 chromosome was associated with DBP ($p = 0.026$) [54] and with BMI [144] The SNP rs671, a missense variant and a classical one known for the phenomenon "Asian flush" or "Asian blush" or "Alcohol flush" in gene ALDH2 (aldehyde dehydrogenase) at 12q24.12 chromosome, causes red face in some individuals after drinking alcohol. This SNP has been published in association with essential hypertension (based on drinking behavior) and BMI/Obesity [145, 146] but the study [147] denies the association of rs671 with essential hypertension. The rs653178 (explained above) in gene ATXN2 has also been reported in relation ($p = 0.006$) with essential hypertension [148] (Table 4).

Common SNPs associated with BMI and IQ

High BMI is considered as a marker of obesity and therefore has association with increased health burden such as Type II Diabetes (T2D) and CVD [149–151]. It is also linked to a decline in cognitive performance, with brain atrophy and T2D being two probable causes [152, 153]. The SNPs rs1535 and rs174575 in FADS2-fatty acid desaturase 2 enzyme have been implicated in moderating the effects of breastfeeding on IQ in several studies with a marginal *p*-value [29, 154, 155]. The FADS2 is a fatty acyl-coenzyme A (CoA) desaturase that introduces a cis double bond at carbon 6 of the fatty acyl chain during the biosynthesis of highly unsaturated fatty acids (HUFA) from the essential polyunsaturated fatty acids (PUFA),

Table 3 SNPs related to BP, chromosomal location, gene, allele, effect of that SNP and other associated traits

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample size	Method/study	References
rs4762	1q42.2	*AGT*	G > A	DBP	0.002	Diabetic nephropathy	2343/546	Candidate	[106]
rs5049	1q42.2	AGT	C > T	Elevate BP	0.00006		2343	Candidate	[107]
rs699	1q42.2	AGT	A > G	RAS system, vasoreactivity	< 0.0001	Diabetic nephropathy Coronary heart disease	1245	Candidate	[107]
rs671	12q24.12	ALDH2	G > A	Increased BMI	3.4×10^{-11}	Hypertension	757/7488–47,352.4204–5435	GWAS	[44, 66]
rs4680	22q11.21	COMT	G > A	Transfers methyl group to catecholamines, to inactivate	< 0.01	Weight gain/decreased SBP	165/6969		[59–61]
rs7138803	12q13.12	FAIM2	G > T G > A	Increased BMI	0.015	WC, obesity, DBP	3077/249796		[54, 62]
rs9939609	16q12.2	FTO	T > A	Increasing BMI	2×10^{-7}	T2D, Obesity, high BP	38,759	GWAS	(102]
rs17782313	18	MC4R	T > A T > C	High BMI	< 0.05	BP, T2D	216		[25–27]
rs2266782	1q24.3	FMO3	G > A	Degrades catecholamines inactivate	3×10^{-11}	Stroke, cardiac dysfunction Renal failure	49	Candidate	[108]
rs17367504	1p36.22	MTHFR-NPPB	A > G	Protect against non-gestational hypertension	3.52×10^{-5}	Proteinuria in pregnancy	1822	GWAS	[109]
rs10938397	4p12	GNPDA2	A > G	Increased BMI	0.00093	DBP, WC, waist-to-height ratio, and fat mass percentage	3077/3503	GWAS	[54]
rs5068	1p36.22	NPPA	A > G, T	Low BP	4×10^{-5}	BMI, metabolic syndrome		Candidate	[30, 31]
rs653178	12	ATXN2	C > G C > T	High BMI	5×10^{-7}	DBP		GWAS	[56]
rs198358	1p36.22	NPPA-A1	T > C	Hypotension	2×10^{-4}	BMI	1507	Candidate	[65, 31]
rs5186	3p21	AGTR1	A > C	Severity on glucose and lipid metabolism	0.0005	CVD, and metabolic syndrome liver disease	314	candidate	[110]
rs4961	4p16.3	ADD1	G > A, T	Body sodium variation/deleterious by having changes in the protein-coding region	1.09×10^{-6}	Heart disease, stroke	1113	Candidate	[111]
rs11191580	10q24.33	NT5C2	T > C	Increased BMI	3.83×10^{-8}	Schizophrenia Bipolar disorder Major depression	86,757/7488–47,354		[44]
rs1173771	5p13.3	NPR3-C5orf23	A > G	Elevate BP	3.26×10^{-25}	Pulse pressure Arterial pressure, BMI-adjusted hip circumference	140,886	GWAS	[112]

Table 3 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample size	Method/study	References
rs1799983	7q36.1	NOS3	T > A, G	EH	2.63×10^{-3}	CAD, myocardial infarction and stroke	260	GWAS	(158]
rs2070744	7q36.1	NOS3	C > T	EH	6.42×10^{-4}	CAD, Myocardial infarction and stroke	260	GWAS	[113]
rs1813353	10p12.31	CACNB2[3']	T > C	DBP	4×10^{-13}	Heart disease diabetes		GWAS	[114]
rs6015450	20q13.32	GNAS-EDN3	A > G	SBP, DBP	0.59, 0.47	Stroke, CAD	787	GWAS	[115]
rs13333226	16p12.3	UMOD	A > G	Reduce urinary uromodulin excretion	3.6×10^{-11}	CVD	39,706	GWAS	[116]
rs4373814	10p12.33	CACNB2[5']	G > C, T	Increased hypertension	9×10^{-9}		1006	GWAS	[117]
rs2681472	12q21.33	ATP2B1	A > G	DBP	3.7×10^{-8}	Metabolic syndrome, arterial stiffness	29,136	GWAS	[118]
rs932764	10p23.33	PLCE1	A > G	Elevate BP	7.1×10^{-16}	CVD	200,000	GWAS	[119]
rs5443	12p13	GNB3	C > T	Enhanced G-protein activation	0.00002	Obesity, Diabetes		Candidate	[28]
rs3749585	4p12	CORIN	A > G	Low density lipoprotein Cholesterol, higher risk ofhypertension	0.029		808	High-resolution melting (HRM)	[120]
rs13306046	19p13.3	TBXA2R	C/T	Reduction in miR-induced repression of gene expression, decreased BP		Myocardial infarction Decreased in BP		Dual luciferase reporter gene system	[121]
rs10757274	9p21	CDKN2B-AS1	A/G	Elevate BP	0.001		350	RT-PCR	[50]
rs2383207	9p21.3	CDKN2B-AS1	A/G	Increased fasting glucose level	0.001	Weight gain	350	RT-PCR	[50]
rs1333049	9p21.3	CDKN2A, CDKN2B	G/C	elevated systolic BP levels	0.047		350	R-PCR	[50]
rs11174811	12q14-15	AVPR1A	C > A	Increased BP	3×10^{-5}	Myocardial infarction			[122]
rs4705342	5q32	CARMN; MIR143	T > C T > G	Associated with the risk of EH	0.009	Diabetes mellitus of ischemic stroke	343	TaqMan assay	[123]
rs17228616	7q22	ACHE, UFSP1	G > T	Minor allele shows elevated blood pressure	< 0.001	Anxiety, hypertension		GWAS	[124]
rs938671	17q21.2	ATP6V0A1	T > C	Hypertension	0.003	Hypertension risk		GWAS	[125]
rs2681492	12q21.33	ATP2B1	A; G/G; G	SBP, DBP	3×10^{-11}	CVD, diabetes	2881	GWAS	[126]
rs8096897	18q21.2	C18or f1		SBP	3.2×10^{-11}		29,136	GWAS	[118]
rs13107325	4p24	SLC39A8		High BP	< 0.05	BMI, intelligence		GWAS	[127]

Table 3 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample size	Method/study	References
rs3184504	12q24.12	SH2B3	T > A T > C T > G	SBP DBP	5×10^{-7}	Coronary heart disease, diabetes mellitus, BMR	29,136	GWAS	[118]
rs880315	1p36.22	CASZ1	T > C T > G	SBP	2.1×10^{-7}	Urinary albumin to creatinine ratio/ischemic stroke	600	GWAS	[128]
rs381815	11p15.2	PLEKHA7	T > C	SBP	5×10^{-7}	Pulse pressure, arterial pressure	34,433	GWAS	[129]
rs7571613	2	C2or f88	A > G	SBP	7.2×10^{-7}		8512	GWAS	[129]
rs7640747	3p22.2	ITGA9	C > G	SBP	4.8×10^{-7}		8512	GWAS	[129]
rs11014166	10p12.31	CACNB2	A > T	DBP/SBP	8.7×10^{-7}		29,136	GWAS	[118]
rs1119154	10q24.3	CYP17A1	C > T	SBP, DBP	0.002		4460	GWAS	[130]
rs11024074	11p15.2	PLEKHA7	T > C	SBP	3.76×10^{-2}		8512	GWAS	[129]
ra11105354	12q21.33	ATP2B1	A > G	SBP	4×10^{-7}		29,136	GWAS	[118]
rs12579302	12q21.33	ATP2B1	A > G	SBP	4×10^{-7}	Coronary heart disease	29,136	GWAS	[118]
rs10757278	9p21.3	CDKN2A, CDKN2B	A > GA > C A > T	Elevate BP	1×10^{-20}	Coronary heart disease, diabetes, myocardial infarction, stroke, obesity	10,881	RT-PCR	[131, 50]
rs5225	14q32.2	BDKRB2	T > A T > C	RAAS-related gene influence BP		Myocardial infarction, arterial pressure	890	SMILE	[121]
rs198358	1p36.22	NPPA-AS1	A > G	Increased circulating natriuretic peptide concentration	8×10^{-30}	Obesity, heart failure risk	14,743	GWAS	[132]
rs1378942	15q24.1	CSK	C > A C > T	Pulse pressure, arterial pressure	4.6×10^{-7}	CVD	14,105		[133]
rs6265	11p14.1	BNDF	C > T	Decreased SBP	0.003	BMI, memory	8842		[134]
rs62011052	15q25.1	ADAMTS7	T/C	Angiotensin II stimulation induced renal expression	3×10^{-15}	Heart disease, diabetes autoimmune disease pulse pressure		GWAS	[114]
rs17249754	12q21.33	ATP2B1	G > A	Increased hypertension, arterial stiffness	4.25×10^{-9}	Pulse pressure, arterial pressure	8842	GWAS	[135]
rs11024102	11p15.2	PLEKHA7	T > A T > C	DBP	5.33×10^{-12}	Glaucoma	29,136	GWAS	[118]
rs2760061	1q42.13	WNT3A	T > A	Agent acting on the RAS system	2×10^{-16}	CVD, SBP diabetes	318,664	GWAS	[136]
rs7129220	11p15.4	AMPD3 Intron variant	G/A	High BP	0.20		38,970		[65]
rs11953630	5q33.3	EBF1 Intergenic variant	C/A/T	Hypotension	< 0.0016		38,970		[65]

Table 3 (continued)

SNP name	Chromosomal location	Gene	Allele	Effect	*p* value	Associated trait	Sample size	Method/study	References
rs805303	6p21.33	BAG6 Intron variant	A/G/C	Hypotension	0.79		38,970		[65]
rs2286672	17p13.2	PLD2, Missense variant	C/T	Significantly decreased SBP recessively SBP	0.038	Systemic Lupus Erythematosus	8842		[134]
rs16835244	1	AZIN2	G > AG > T	Hypertension/SBP	0.002		8842		[134]
rs4963	4	ADD1	C > G C > T	Hypertension	0.001		5097, 5937		[137]
rs2288774	18	NEDD4L	CC- or CT	SBP	0.01		4001		[103]
rs4149601	18	NEDD4L	G > A	DBP	0.03		4001 s		[103]
rs3794260	12	KIAA0789	G/A	Hypertension	0.0001		752 hypertensive and 752 normotensive subjects		[104]
rs9739493	12	KIAA0789	T/C		0.0001		752 hypertensive and 752 normotensive subjects		[104]
rs4757391	11p15.2	SOX6	T > C	DBP	5×10^{-9}		11,816	GWAS	[138]

Table 4 Common SNPs for QTs selected in the present study in different combinations

SNPs	Chromosome	Gene	Gene variant
Common SNPs related to BMI and IQ			
rs1535	11q12.2	FADS2	Intron variant
rs174575	11q12.2	FADS2	Intron variant
Common SNPs related to IQ and BP			
No SNPs	–	–	–
Common SNPs related to BMI and BP			
rs5068	1p36.22	NPPA	3′utr region
rs2383207	9p21.3	CDKN2B-AS1	Intron variant
rs5443	12p13	GNB3	Synonymous variant
rs9939609	16q12.2	FTO	Intron variant
rs17782313	18q21.3	MCAR	Intergenic variant
rs10938397	4p12	GNPDA2	Intergenic variant
rs671	12q24.12	ALDH2	Missense variant
rs7138803	12q13.2	FAIM2	Intergenic variant
rs198358	1p36.22	NPPA	3′utr region
rs653178	12q24.12	ATXN2	Intron variant
rs11191580	10q24.33	NT5C2	Intron variant
Common SNPs identified for all three QTs, viz. BMI, IQ and BP			
rs6265	11p14.1	BDNF	Missense variant
rs4680	22q11.21	COMT	Missense variant
rs13107325	4p24	SLC39A8	Missense variant

linoleic acid and alpha-linolenic acid precursors [156]. Breastfeeding indicates to be connected with higher IQ in observational studies and randomized controlled trials, presumably because breast milk contains long-chain PUFA [155]. The well-studied SNP rs4680 (Missense variant = Val158Met) in COMT-Catechol-*O*-methyltransferase gene occurs at 22q11.21 chromosome. The COMT gene produces the COMT enzyme, which degrades dopamine in the prefrontal cortex of the brain. The wild-type allele is a (G), which codes for valine; the (A) alteration polymorphism switches valine to methionine. The configuration of the resulting enzyme is changed, and its functionality is reduced to 25% of that of wild type [157]. Multiple studies indicates the involvement of this SNP in decrease in IQ as maternal anxiety increase [59], and in neurological disorders i.e., bipolar disorder [158] schizophrenia [159, 160] Alzheimer's disease [161] and psychiatric disorders [162]. This variant is also known to be involved in increment of BMI ($p = 0.002$) [163]. In another empirical study, 1,000 random drawings of 812 and 6649 SNPs from the 2,475,536 variations yielded an overlap of 7 or more SNPs on seven occasions, showing a substantial enrichment for hits ($p = 0.007$). The seven SNPs found were in four genes: AKAP6 (rs17522122), TOMM40 (rs2075650), TMEM161B (rs2410767, rs6870983, rs7445169) and TNRC6B (rs2410767, rs6870983, rs7445169) (rs4820408, rs8142495). With the exception of the TOMM40 variant (rs429358), the impact sizes for SNPs in concern were in reverse direction (variants that are significantly linked with general cognitive function are inversely associated with BMI) [164]. Furthermore, a recent study found a link between a higher BMI and a decreased risk of dementia. Both cognitive performance and BMI have been shown to be influenced by genetic factors in studies [93, 165–167] (Table 4).

Common SNPs associated with BP and IQ

Hypertension and/or increments in BP (systolic, diastolic or mean atrial pressure (MAP)) were statistically significant predictors of progressive decline in Cognitive performance (linear and nonlinear) over time. The hypertension and BP-associated decline in cognitive performance reported in these studies were seen with control for stroke, dementia, CVD risk factors, comorbidity and antihypertensive treatment [168]. The consequences of pediatric hypertension on the nervous system have been detailed in a study, with acute neurological involvement ranging from posterior reversible encephalopathy syndrome to infarction and hemorrhage. Learning difficulties and executive function deficits are common in children with chronic hypertension, which may be treatable with antihypertensive therapy [169]. A population-based

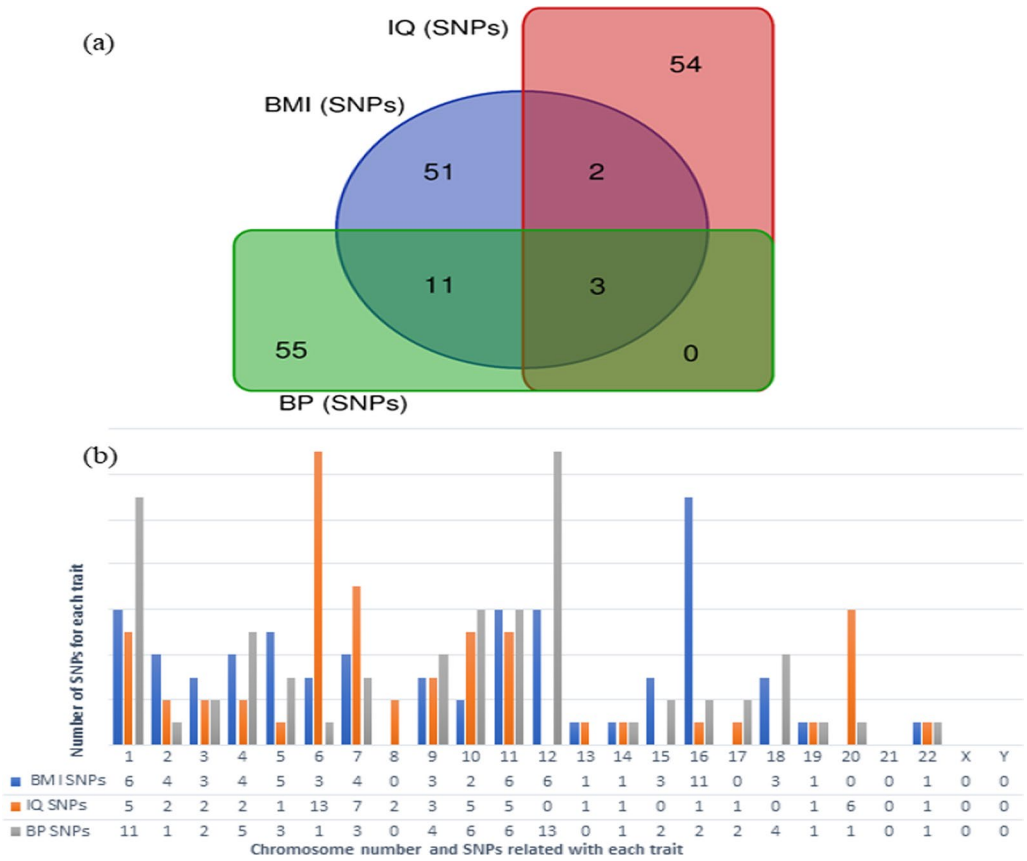

Fig. 1 **a** Venn diagram showing the number of SNPs associated with BMI, IQ and BP (individually and in combinations). It is evident from picture that 51, 54 and 55 SNPs associated only with BMI, IQ and BP respectively, 11 common SNPs for BP and BMI, 2 common SNPs for IQ and BMI and no common SNP for BP and IQ. Only 3 SNPs are common for all three traits. **b** Bar graph showing the number of SNPs for each trait and their location on chromosomes

GWAS found a probable association between hypotension and cognitive impairment in healthy elderly adults. With the exception of rs117129097, which was connected to hypotension, LRRTM4 (rs13388459, rs1075716, rs62171995, rs17406146, rs2077823 and rs62170897), PCSK5 (rs10521467) and the intergenic SNP rs117129097 were shown to be markers for cognitive impairment (CI), coexisting with hypotension in the current study. Inadequate cerebral perfusion, loss of autoregulation, and endothelial dysfunction in the neurovascular unit are suggested to be the processes of hypotension-related CI, which leads to microvascular pathology, stroke, and the accumulation of Aβ protein and neurofibrillary tangles. The removal of Aβ from the brain is affected by vascular reactivity, which is altered by microvascular illness [170–172] (Table 4).

Common SNPs associated with BMI, IQ and BP

We discovered three different SNPs involving in these three QTs (BMI, IQ and BP). First, the rs6265 in the BDNF gene, second the rs13107325 in the SL39A8 gene, and third is rs4680 in the COMT gene. The neurotrophin brain-derived neurotrophic factor (BDNF) is abundantly present and highly expressed in brain. This growth factor influences a variety of brain processes related to plasticity and repair [173]. The BDNF polymorphism has been associated to motor learning, short-term plasticity, and the operation of the human brain's motor system. Val66Me is another name for this variant, in which the G allele codes for Val and the A allele codes for Met. The people not having this polymorphism, (Val/Val condition) have larger baseline activation volumes (including

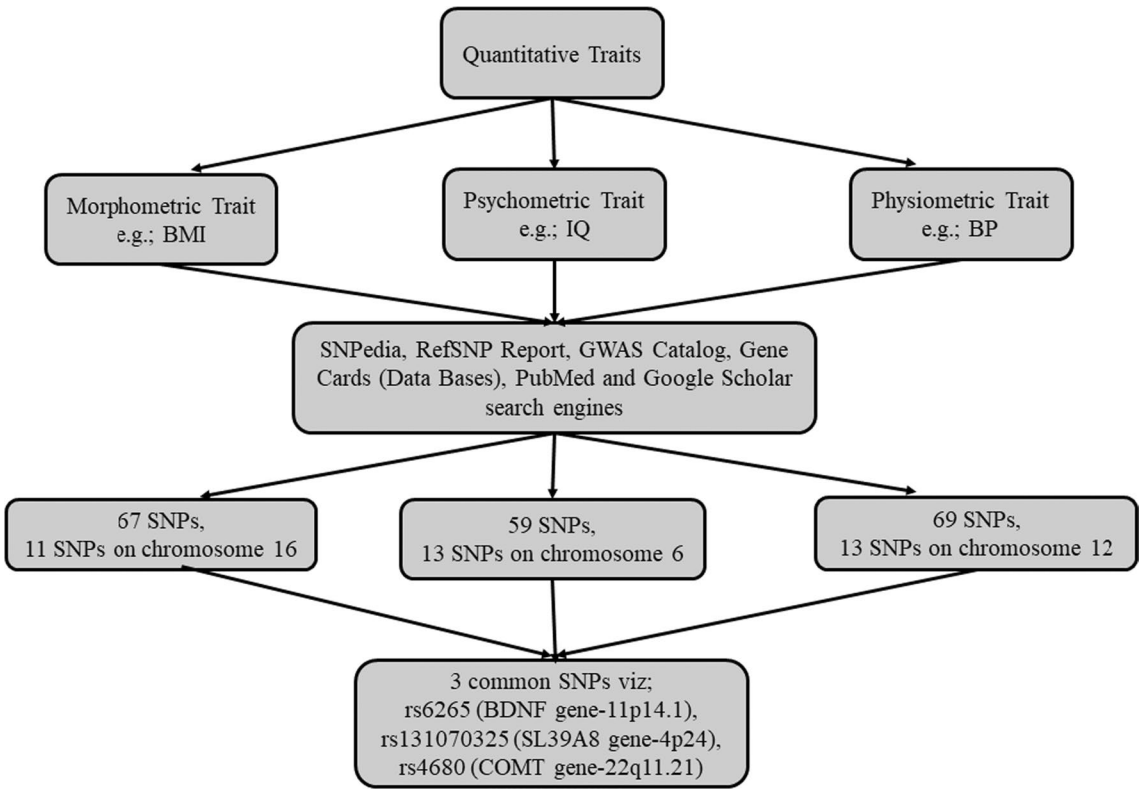

Fig. 2 Flowchart depicting the summary of the present study

inside bilateral sensorimotor cortex) than those having Met condition [85] BP has also been studied in correlation with this SNP rs6265, with a significant reduction in SBP [129]. Another study on this SNP also found a strong association of this SNP to current BMI and change in BMI. The Current BMI is defined as the BMI calculated using self-reported current weight and height, as well as BMI change (per year) calculated using (current BMI–BMI at 20)/(age-20) [39]. Another SNP, the SLC39A839 gene is a member of the SLC39 family of solute carrier genes. This gene is located on chromosome 4p24, and rs13107325, a missense variant, has been associated to high BP and BMI [26, 127]. Poorer scores were connected to the rs13107325 minor allele (T; lower blood Mn). As a result, genotypes linked to greater blood Mn performed worse on specific IQ subtests, had more sway, and were rated as having more behavioral issues. Mn levels in the blood have been connected to cognitive, behavioral, motor, and sway outcomes in children [96] (Fig. 1a, b; Table 4).

Conclusion

The majority of biological processes important to human health and medicine, such as height, weight, obesity, IQ and diabetes, are quantitative or complex features. Quantitative qualities are regulated by a large number of genes, each of which has a minor effect and is easily changed by environmental circumstances. The genes that affect a QTs have a large impact, whereas others have a minor impact. The purpose of this study was to use review/research articles all around the world to uncover common SNPs or genes for three quantitative variables in human population (BMI, IQ, BP or hypertension). As a result, we gathered more than 58 significantly linked SNPs for each attribute separately and looked for common SNPs among them. Following that, we discovered 11 common SNPs for BMI/BP, 2 for BMI/IQ and no common SNPs BP/IQ, because the SNPs which were common in BP/IQ were also common for all three traits.

Consequently, we discovered 3 common SNPs in populations for all three QTs, viz. SNP rs6265 at the BDNF gene on chromosome 11p14.1 and SNP rs131070325 at the SL39A8 gene on chromosome 4p24, and SNP rs4680 at the COMT gene on chromosome 22q11.21. By arranging the SNPs according to their location on chromosome we found that most of the SNPs (11) for BMI are present on chromosome 16, 13 SNPs of IQ on chromosome 6 and 13 SNPs for BP on chromosome 12 (Fig. 2).

In our review, we focused on the common SNPs and gene expression activities that influence these three quantitative traits. If these SNPs are found in any population, we can get prior knowledge about the trait associated with these variations before the manifestation of that feature. The most common clinical use of SNPs is to determine illness susceptibility and evaluate the success of pharmacological therapy tailored to an individual's need, as well as to identify disease susceptibility genes. These SNPs would able to be used as population screening markers for these three quantitative features and therefore crucial for improving human health and country's pharmaceutical condition in India. Perhaps with more research or a meta-analysis, new SNPs important to this will be uncovered. Finally, the outcome of our work may be used to locate common SNPs and genes across the genome that regulate these three quantitative traits.

Abbreviations

AMPD3: Adenosine monophosphate deaminase 3; AZIN: Antizyme inhibitor; BDNF: Brain-derived neurotrophic factor; BMI: Body mass index; BP: Blood pressure; CAD: Coronary artery disease; CI: Cognitive impairment; COMT: Catechol-o-methyl transferase; CVD: Cardiovascular disease; DBP: Diastolic blood pressure; FIQ: Functional intelligence quotient; FOXO3: Forkhead box O3; FSIQ: Full-scale intelligence quotient; GIPR: Gastric inhibitory polypeptide receptor; GWAS: Genome-wide association studies; GxE: Genotype–environmental interaction; HIP1: Huntingtin-interacting protein 1; HUFA: Highly unsaturated fatty acid; IQ: Intelligence quotient; MAP: Mean arterial pressure; PIQ: Performance intelligence quotient; PUFA: Polyunsaturated fatty acid; QTs: Quantitative traits; SBP: Systolic blood pressure; SLC: Solute carrier; SNP: Single nucleotide polymorphism; T2D: Type 2 diabetes; VAT: Visceral adipose tissue; VIQ: Verbal intelligence quotient; WC: Waist circumference.

Acknowledgements

The authors are grateful to the Chairman, Department of Zoology, AMU, Professor Mohammad Afzal for providing necessary laboratory facilities.

Authors' contributions

WC did conceptualization, data curation, investigation, methodology, writing—review, and formal analysis; RF did formal analysis, investigation, conceptualization and writing—review; AW did data curation, investigation and writing—review and editing; MA did conceptualization, methodology, investigation and supervision. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 22 December 2021 Accepted: 21 February 2022
Published online: 08 March 2022

References

1. Alwi ZB (2005) The use of SNPs in pharmacogenomics studies. Malays J Med Sci MJMS 12(2):4–12
2. 1000 Genomes Project Consortium, Auton A, Brooks LD, Durbin RM, Garrison EP, Kang HM et al (2015) A global reference for human genetic variation. Nature 526(7571):68–74
3. Magner D, Biala E, Lisowiec-Wachnicka J, Kierzek E, Kierzek R (2015) A tandem oligonucleotide approach for SNP-selective RNA degradation using modified antisense oligonucleotides. PLoS ONE 10(11):e0142139
4. Khanna D, Yates Z (2019) Body Mass Index: A Critical Review Obesity. J Obes Weight Loss Ther 2:382
5. Ganuthula VRR, Sinha S (2019) The looking glass for intelligence quotient tests: the interplay of motivation, cognitive functioning, and affect. Front Psychol 10:2857
6. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF et al (2018) Hypertension. Nat Rev Dis Primer 22(4):18014
7. Chen R, Dharmarajan K, Kulkarni VT, Punnanithinont N, Gupta A, Bikdeli B et al (2013) Most important outcomes research papers on hypertension. Circ Cardiovasc Qual Outcomes 6(4):e26-35
8. Hossain FB, Adhikary G, Chowdhury AB, Shawon MSR (2019) Association between body mass index (BMI) and hypertension in south Asian population: evidence from nationally-representative surveys. Clin Hypertens 25(1):28
9. Landi F, Calvani R, Picca A, Tosato M, Martone AM, Ortolani E et al (2018) Body mass index is strongly associated with hypertension: results from the longevity check-up 7+ study. Nutrients 10(12):1976
10. Robertson JIS (2004) Childhood intelligence and blood pressure in middle age. J Hypertens 22(5):871
11. Lyngdoh T, Viswanathan B, Kobrosly R, van Wijngaarden E, Huber B, Davidson PW et al (2013) Blood pressure and cognitive function: a prospective analysis among adolescents in Seychelles. J Hypertens 31(6):1175–1182
12. Lande MB, Kupferman JC (2019) Blood pressure and cognitive function in children and adolescents. Hypertension 73(3):532–540
13. Sellier C, Campanari M, Julie Corbier C, Gaucherot A, Kolb-Cheynel I, Oulad-Abdelghani M et al (2016) Loss of C9 ORF 72 impairs autophagy and synergizes with polyQ Ataxin-2 to induce motor neuron dysfunction and cell death. EMBO J 35(12):1276–1297
14. Figueroa KP, Farooqi S, Harrup K, Frank J, O'Rahilly S, Pulst SM (2009) Genetic variance in the spinocerebellar ataxia type 2 (ATXN2) gene in children with severe early onset obesity. PLoS ONE 4(12):e8280
15. Halbach MV, Gispert S, Stehning T, Damrath E, Walter M, Auburger G (2017) Atxn2 knockout and CAG42-knock-in cerebellum shows similarly dysregulated expression in calcium homeostasis pathway. Cerebellum 16(1):68–81
16. Meierhofer D, Halbach M, Şen NE, Gispert S, Auburger G (2016) Ataxin-2 (Atxn2)-knock-out mice show branched chain amino acids and fatty acids pathway alterations. Mol Cell Proteom 15(5):1728–1739
17. Lv W-Q, Zhang X, Zhang Q, He J-Y, Liu H-M, Xia X et al (2017) Novel common variants associated with body mass index and coronary artery

disease detected using a pleiotropic cFDR method. J Mol Cell Cardiol 112:1–7
18. Miyawaki K, Yamada Y, Yano H, Niwa H, Ban N, Ihara Y et al (1999) Glucose intolerance caused by a defect in the entero-insular axis: a study in gastric inhibitory polypeptide receptor knockout mice. Proc Natl Acad Sci 96(26):14843–14847
19. Gong J, Nishimura KK, Fernandez-Rhodes L, Haessler J, Bien S, Graff M et al (2018) Trans-ethnic analysis of metabochip data identifies two new loci associated with BMI. Int J Obes 42(3):384–390
20. Abadi A, Alyass A, Robiou du Pont S, Bolker B, Singh P, Mohan V et al (2017) Penetrance of polygenic obesity susceptibility loci across the body mass index distribution. Am J Hum Genet 101(6):925–938
21. Graff M, Scott RA, Justice AE, Young KL, Feitosa MF, Barata L et al (2017) Genome-wide physical activity interactions in adiposity—a meta-analysis of 200,452 adults. PLoS Genet 13(4):e1006528
22. Heid IM, Vollmert C, Kronenberg F, Huth C, Ankerst DP, Luchner A et al (2008) Association of the MC4R V103I polymorphism with the metabolic syndrome: the KORA study. Obes Silver Spring Md 16(2):369–376
23. Vimaleswaran KS, Li S, Zhao JH, Luan J, Bingham SA, Khaw K-T et al (2009) Physical activity attenuates the body mass index-increasing influence of genetic variation in the FTO gene. Am J Clin Nutr 90(2):425–428
24. Hinney A, Nguyen TT, Scherag A, Friedel S, Brönner G, Müller TD et al (2007) Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. PLoS ONE 2(12):e1361
25. Marcadenti A, Fuchs FD, Matte U, Sperb F, Moreira LB, Fuchs SC (2013) Effects of FTO RS9939906 and MC4R RS17782313 on obesity, type 2 diabetes mellitus and blood pressure in patients with hypertension. Cardiovasc Diabetol 12(12):103
26. Speliotes EK, Willer CJ, Berndt SI, Monda KL, Thorleifsson G, Jackson AU et al (2010) Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. Nat Genet 42(11):937–948
27. Yu K, Li L, Zhang L, Guo L, Wang C (2020) Association between MC4R rs17782313 genotype and obesity: a meta-analysis. Gene 733:144372
28. Siffert W (2003) G-protein β3 subunit 825T allele and hypertension. Curr Hypertens Rep 5(1):47–53
29. Caspi A, Williams B, Kim-Cohen J, Craig IW, Milne BJ, Poulton R et al (2007) Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism. Proc Natl Acad Sci USA 104(47):18860–18865
30. Cannone V, Cefalu' AB, Noto D, Scott CG, Bailey KR, Cavera G et al (2013) The atrial natriuretic peptide genetic variant rs5068 is associated with a favorable cardiometabolic phenotype in a Mediterranean population. Diabetes Care 36(9):2850–2856
31. Zhang H, Mo X, Zhou Z, Zhu Z, Huangfu X, Xu T et al (2018) Smoking modifies the effect of two independent SNPs rs5063 and rs198358 of NPPA on central obesity in the Chinese Han population. J Genet 97(4):987–994
32. de la Garza Puentes A, Montes Goyanes R, Chisaguano Tonato AM, Torres-Espínola FJ, Arias García M, de Almeida L et al (2017) Association of maternal weight with FADS and ELOVL genetic variants and fatty acid levels- The PREOBE follow-up. PLoS ONE 12(6):35
33. Zobel DP, Andreasen CH, Grarup N, Eiberg H, Sørensen TIA, Sandbaek A et al (2009) Variants near MC4R are associated with obesity and influence obesity-related quantitative traits in a population of middle-aged people: studies of 14,940 Danes. Diabetes 58(3):757–764
34. Sung YJ, Pérusse L, Sarzynski MA, Fornage M, Sidney S, Sternfeld B et al (2016) Genome-wide association studies suggest sex-specific loci associated with abdominal and visceral fat. Int J Obes 40(4):662–674
35. Johansson A, Marroni F, Hayward C, Franklin CS, Kirichenko AV, Jonasson I et al (2010) Linkage and genome-wide association analysis of obesity-related phenotypes: association of weight with the MGAT1 gene. Obes Silver Spring Md 18(4):803–808
36. Widén E, Ripatti S, Cousminer DL, Surakka I, Lappalainen T, Järvelin M-R et al (2010) Distinct variants at LIN28B influence growth in height from birth to adulthood. Am J Hum Genet 86(5):773–782
37. Hunt SC, Stone S, Xin Y, Scherer CA, Magness CL, Iadonato SP et al (2008) Association of the FTO gene with BMI. Obes Silver Spring Md 16(4):902–904
38. Jacobsson JA, Rask-Andersen M, Risérus U, Moschonis G, Koumpitski A, Chrousos GP et al (2012) Genetic variants near the MGAT1 gene are associated with body weight, BMI and fatty acid metabolism among adults and children. Int J Obes 36(1):119–129
39. Iwase M, Matsuo K, Nakatochi M, Oze I, Ito H, Koyanagi Y et al (2021) Differential effect of polymorphisms on body mass index across the life course of Japanese: the Japan multi-institutional collaborative cohort study. J Epidemiol 31(3):172–179
40. Corella D, Lai C-Q, Demissie S, Cupples LA, Manning AK, Tucker KL et al (2007) APOA5 gene variation modulates the effects of dietary fat intake on body mass index and obesity risk in the Framingham Heart Study. J Mol Med Berl Ger 85(2):119–128
41. Wang T, Moon J-Y, Wu Y, Amos CI, Hung RJ, Tardon A et al (2017) Pleiotropy of genetic variants on obesity and smoking phenotypes: results from the Oncoarray Project of The International Lung Cancer Consortium. PLoS ONE 12(9):e0185660
42. Kamura Y, Iwata M, Maeda S, Shinmura S, Koshimizu Y, Honoki H et al (2016) FTO gene polymorphism is associated with type 2 diabetes through its effect on increasing the maximum BMI in Japanese men. PLoS ONE 11(11):e0165523
43. Laber S, Cox RD (2015) Commentary: FTO obesity variant circuitry and adipocyte browning in humans. Front Genet 6:318
44. Wen W, Zheng W, Okada Y, Takeuchi F, Tabara Y, Hwang J-Y et al (2014) Meta-analysis of genome-wide association studies in East Asian-ancestry populations identifies four new loci for body mass index. Hum Mol Genet 23(20):5492–5504
45. Liu Y, Liu Z, Song Y, Zhou D, Zhang D, Zhao T et al (2010) Meta-analysis added power to identify variants in FTO associated with type 2 diabetes and obesity in the Asian population. Obes Silver Spring Md 18(8):1619–1624
46. Fawcett KA, Barroso I (2010) The genetics of obesity: FTO leads the way. Trends Genet TIG 26(6):266–274
47. Wang N, Lu M, Chen C, Xia F, Han B, Li Q et al (2018) Adiposity genetic risk score modifies the association between blood lead level and body mass index. J Clin Endocrinol Metab 103(11):4005–4013
48. Han L, Tang L, Wang C, Chen Z, Zhang T, Chen S et al (2014) Fat mass and obesity-associated gene rs11642015 polymorphism is significantly associated with prediabetes and type 2 diabetes subsequent to adjustment for body mass index. Biomed Rep 2(5):681–686
49. Fu J, Li G, Li L, Yin J, Cheng H, Han L et al (2017) The role of established East Asian obesity-related loci on pediatric leptin levels highlights a neuronal influence on body weight regulation in Chinese children and adolescents: the BCAMS study. Oncotarget 8(55):93593–93607
50. Bayoglu B, Yuksel H, Cakmak HA, Dirican A, Cengiz M (2016) Polymorphisms in the long non-coding RNA CDKN2B-AS1 may contribute to higher systolic blood pressure levels in hypertensive patients. Clin Biochem 49(10–11):821–827
51. Mitchell JA, Hakonarson H, Rebbeck TR, Grant SFA (2013) Obesity-susceptibility loci and the tails of the pediatric BMI distribution. Obes Silver Spring Md 21(6):1256–1260
52. Ruiz-Narváez EA, Haddad SA, Rosenberg L, Palmer JR (2016) Birth weight modifies the association between central nervous system gene variation and adult body mass index. J Hum Genet 61(3):193–198
53. Ibáñez-Zamacona ME, Poveda A, Rebato E (2019) Contribution of obesity associated genetic variants to anthropometric somatotype components. Anthropol Anz Ber Uber Biol-Anthropol Lit 76(2):101–111
54. Xi B, Zhao X, Shen Y, Wu L, Hotta K, Hou D et al (2013) Associations of obesity susceptibility loci with hypertension in Chinese children. Int J Obes 37(7):926–930
55. Rode L, Nordestgaard BG, Weischer M, Bojesen SE (2014) Increased body mass index, elevated C-reactive protein, and short telomere length. J Clin Endocrinol Metab 99(9):E1671-1675
56. Ninomiya-Baba M, Matsuo J, Sasayama D, Hori H, Teraishi T, Ota M et al (2017) Association of body mass index-related single nucleotide polymorphisms with psychiatric disease and memory performance in a Japanese population. Acta Neuropsychiatr 29(5):299–308
57. Okada Y, Kubo M, Ohmiya H, Takahashi A, Kumasaka N, Hosono N et al (2012) Common variants at CDKAL1 and KLF9 are associated with body mass index in east Asian populations. Nat Genet 44(3):302–306

58. Costa-Urrutia P, Abud C, Franco-Trecu V, Colistro V, Rodríguez-Arellano ME, Alvarez-Fariña R et al (2020) Effect of 15 BMI-associated polymorphisms, reported for Europeans, across ethnicities and degrees of Amerindian ancestry in Mexican children. Int J Mol Sci 21(2):E374
59. O'Donnell KJ, Glover V, Lahti J, Lahti M, Edgar RD, Räikkönen K et al (2017) Maternal prenatal anxiety and child COMT genotype predict working memory and symptoms of ADHD. PLoS ONE 12(6):e0177506
60. Secher A, Bukh J, Bock C, Koefoed P, Rasmussen HB, Werge T et al (2009) Antidepressive-drug-induced bodyweight gain is associated with polymorphisms in genes coding for COMT and TPH1. Int Clin Psychopharmacol 24(4):199–203
61. Xu J, Boström AE, Saeed M, Dubey RK, Waeber G, Vollenweider P et al (2017) A genetic variant in the catechol-O-methyl transferase (COMT) gene is related to age-dependent differences in the therapeutic effect of calcium-channel blockers. Medicine (Baltimore) 96(30):e7029
62. Hong KW, Oh B (2012) Recapitulation of genome-wide association studies on body mass index in the Korean population. Int J Obes 36(8):1127–1130
63. Rask-Andersen M, Jacobsson JA, Moschonis G, Ek AE, Chrousos GP, Marcus C et al (2012) The MAP2K5-linked SNP rs2241423 is associated with BMI and obesity in two cohorts of Swedish and Greek children. BMC Med Genet 17(13):36
64. Kitamoto A, Kitamoto T, Mizusawa S, Teranishi H, So R, Matsuo T et al (2013) NUDT3 rs206936 is associated with body mass index in obese Japanese women. Endocr J 60(8):991–1000
65. Fedorowski A, Franceschini N, Brody J, Liu C, Verwoert GC, Boerwinkle E et al (2012) Orthostatic hypotension and novel blood pressure-associated gene variants: genetics of postural hemodynamics (GPH) Consortium. Eur Heart J 33(18):2331–2341
66. Kato N, Takeuchi F, Tabara Y, Kelly TN, Go MJ, Sim X et al (2011) Meta-analysis of genome-wide association studies identifies common variants associated with blood pressure variation in east Asians. Nat Genet 43(6):531–538
67. Bulayeva K, Lesch K-P, Bulayev O, Walsh C, Glatt S, Gurgenova F et al (2015) Genomic structural variants are linked with intellectual disability. J Neural Transm 122(9):1289–1301
68. Benyamin B, Pourcain B, Davis OS, Davies G, Hansell NK, Brion M-JA et al (2014) Childhood intelligence is heritable, highly polygenic and associated with FNBP1L. Mol Psychiatry 19(2):253–258
69. Sniekers S, Stringer S, Watanabe K, Jansen PR, Coleman JRI, Krapohl E et al (2017) Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. Nat Genet 49(7):1107–1112
70. Luciano M, Miyajima F, Lind PA, Bates TC, Horan M, Harris SE et al (2009) Variation in the dysbindin gene and normal cognitive function in three independent population samples. Genes Brain Behav 8(2):218–227
71. Pan Y, Wang K-S, Aragam N (2011) NTM and NR3C2 polymorphisms influencing intelligence: family-based association studies. Prog Neuropsychopharmacol Biol Psychiatry 35(1):154–160
72. Gosso MF, van Belzen M, de Geus EJC, Polderman JC, Heutink P, Boomsma DI et al (2006) Association between the CHRM2 gene and intelligence in a sample of 304 Dutch families. Genes Brain Behav 5(8):577–584
73. Andrews SJ, Das D, Anstey KJ, Easteal S (2017) Association of AKAP6 and MIR2113 with cognitive performance in a population-based sample of older adults. Genes Brain Behav 16(4):472–478
74. Rietveld CA, Esko T, Davies G, Pers TH, Turley P, Benyamin B et al (2014) Common genetic variants associated with cognitive performance identified using the proxy-phenotype method. Proc Natl Acad Sci USA 111(38):13790–13794
75. Piffer D (2015) Estimating the genotypic intelligence of populations and assessing the impact of socioeconomic factors and migrations. The Winnower [Internet]. [cited 2021 Sep 21]; Available from: https://thewinnower.com//papers/estimating-the-genotypic-intelligence-of-populations-and-assessing-the-impact-of-socioeconomic-factors-and-migrations
76. Greenbaum L, Ravona-Springer R, Livny A, Shelly S, Sharvit-Ginon I, Ganmore I et al (2019) The CADM2 gene is associated with processing speed performance—evidence among elderly with type 2 diabetes. World J Biol Psychiatry Off J World Fed Soc Biol Psychiatry 20(7):577–583
77. Zinkstok JR, de Wilde O, van Amelsvoort TAMJ, Tanck MW, Baas F, Linszen DH (2007) Association between the DTNBP1 gene and intelligence: a case-control study in young patients with schizophrenia and related disorders and unaffected siblings. Behav Brain Funct BBF 20(3):19
78. Dick DM, Aliev F, Kramer J, Wang JC, Hinrichs A, Bertelsen S et al (2007) Association of CHRM2 with IQ: converging evidence for a gene influencing intelligence. Behav Genet 37(2):265–272
79. Rolstad S, Pålsson E, Ekman CJ, Eriksson E, Sellgren C, Landén M (2015) Polymorphisms of dopamine pathway genes NRG1 and LMX1A are associated with cognitive performance in bipolar disorder. Bipolar Disord 17(8):859–868
80. Thomson PA, Harris SE, Starr JM, Whalley LJ, Porteous DJ, Deary IJ (2005) Association between genotype at an exonic SNP in DISC1 and normal cognitive aging. Neurosci Lett 389(1):41–45
81. Zhang S, Zhang J (2016) The association of DRD2 with insight problem solving. Front Psychol 7:1865
82. Milnik A, Heck A, Vogler C, Heinze H-J, de Quervain DJ-F, Papassotiropoulos A (2012) Association of KIBRA with episodic and working memory: a meta-analysis. Am J Med Genet Part B Neuropsychiatr Genet Off Publ Int Soc Psychiatr Genet 159B(8):958–969
83. Schneider A, Huentelman MJ, Kremerskothen J, Duning K, Spoelgen R, Nikolich K (2010) KIBRA: A new gateway to learning and memory? Front Aging Neurosci 2:4
84. Gosso MF, de Geus EJC, Polderman TJC, Boomsma DI, Heutink P, Posthuma D (2008) Common variants underlying cognitive ability: further evidence for association between the SNAP-25 gene and cognition using a family-based study in two independent Dutch cohorts. Genes Brain Behav 7(3):355–364
85. McHughen SA, Rodriguez PF, Kleim JA, Kleim ED, Marchal Crespo L, Procaccio V et al (2010) BDNF val66met polymorphism influences motor system function in the human brain. Cereb Cortex 20(5):1254–1262
86. Hashimoto R, Noguchi H, Hori H, Ohi K, Yasuda Y, Takeda M et al (2009) Association between the dysbindin gene (DTNBP1) and cognitive functions in Japanese subjects. Psychiatry Clin Neurosci 63(4):550–556
87. Gosso MF, de Geus EJC, van Belzen MJ, Polderman TJC, Heutink P, Boomsma DI et al (2006) The SNAP-25 gene is associated with cognitive ability: evidence from a family-based study in two independent Dutch cohorts. Mol Psychiatry 11(9):878–886
88. Kuningas M, Putters M, Westendorp RGJ, Slagboom PE, van Heemst D (2007) SIRT1 gene, age-related diseases, and mortality: the Leiden 85-plus study. J Gerontol A Biol Sci Med Sci 62(9):960–965
89. Rietveld CA, Medland SE, Derringer J, Yang J, Esko T, Martin NW et al (2013) GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. Science 340(6139):1467–1471
90. Zhang J-P, Burdick KE, Lencz T, Malhotra AK (2010) Meta-analysis of genetic variation in DTNBP1 and general cognitive ability. Biol Psychiatry 68(12):1126–1133
91. Gosso FM, de Geus EJC, Polderman TJC, Boomsma DI, Posthuma D, Heutink P (2007) Exploring the functional role of the CHRM2 gene in human cognition: results from a dense genotyping and brain expression study. BMC Med Genet 8(8):66
92. Smajlagić D, Kvarme Jacobsen K, Myrum C, Haavik J, Johansson S, Zayats T (2018) Moderating effect of mode of delivery on the genetics of intelligence: explorative genome-wide analyses in ALSPAC. Brain Behav 8(12):e01144
93. Davies G, Armstrong N, Bis JC, Bressler J, Chouraki V, Giddaluru S et al (2015) Genetic contributions to variation in general cognitive function: a meta-analysis of genome-wide association studies in the CHARGE consortium (N=53949). Mol Psychiatry 20(2):183–192
94. Zabaneh D, Krapohl E, Gaspar HA, Curtis C, Lee SH, Patel H et al (2018) A genome-wide association study for extremely high intelligence. Mol Psychiatry 23(5):1226–1232
95. Houlihan LM, Harris SE, Luciano M, Gow AJ, Starr JM, Visscher PM et al (2009) Replication study of candidate genes for cognitive abilities: the Lothian Birth Cohort 1936. Genes Brain Behav 8(2):238–247
96. Wahlberg KE, Guazzetti S, Pineda D, Larsson SC, Fedrighi C, Cagna G et al (2018) Polymorphisms in manganese transporters SLC30A10 and SLC39A8 are associated with children's neurodevelopment by influencing manganese homeostasis. Front Genet 9:664

97. Hagman J, Belanger C, Travis A, Turck CW, Grosschedl R (1993) Cloning and functional characterization of early B-cell factor, a regulator of lymphocyte-specific gene expression. Genes Dev 7(5):760–773
98. LifeLines Cohort Study, EchoGen consortium, AortaGen Consortium, CHARGE Consortium Heart Failure Working Group, KidneyGen consortium, CKDGen consortium et al (2011) Genome-wide association study identifies six new loci influencing pulse pressure and mean arterial pressure. Nat Genet 43(10):1005–1011
99. Binici J, Koch J (2014) BAG-6, a jack of all trades in health and disease. Cell Mol Life Sci 71(10):1829–1837
100. Rasila T, Lehtonen A, Kanerva K, Mäkitie LT, Haglund C, Andersson LC (2016) Expression of ODC antizyme inhibitor 2 (AZIN2) in human secretory cells and tissues. PLoS ONE 11(3):e0151175
101. Kelly TN, Rice TK, Gu D, Hixson JE, Chen J, Liu D et al (2009) Novel genetic variants in the α-adducin and guanine nucleotide binding protein β-polypeptide 3 genes and salt sensitivity of blood pressure. Am J Hypertens 22(9):985–992
102. Dahlberg J, Nilsson L-O, von Wowern F, Melander O (2007) Polymorphism in NEDD4L Is associated with increased salt sensitivity, reduced levels of P-renin and increased levels of Nt-proANP. PLoS ONE 2(5):e432
103. Fava C, von Wowern F, Berglund G, Carlson J, Hedblad B, Rosberg L et al (2006) 24-h ambulatory blood pressure is linked to chromosome 18q21-22 and genetic variation of NEDD4L associates with cross-sectional and longitudinal blood pressure in Swedes. Kidney Int 70(3):562–569
104. Kato N, Miyata T, Tabara Y, Katsuya T, Yanai K, Hanada H et al (2008) High-density association study and nomination of susceptibility genes for hypertension in the Japanese National Project. Hum Mol Genet 17(4):617–627
105. Lule SA, Mentzer AJ, Namara B, Muwenzi AG, Nassanga B, kizito D et al (2019) A genome-wide association and replication study of blood pressure in Ugandan early adolescents. Mol Genet Genomic Med. 2019 Oct [cited 2021 Oct 2];7(10). Available from: https://onlinelibrary.wiley.com/doi/https://doi.org/10.1002/mgg3.950
106. Vázquez-Moreno M, Locia-Morales D, Peralta-Romero J, Sharma T, Meyre D, Cruz M et al (2021) AGT rs4762 is associated with diastolic blood pressure in Mexicans with diabetic nephropathy. J Diabetes Complicat 35(3):107826
107. Soltész B, Pikó P, Sándor J, Kósa Z, Ádány R, Fiatal S (2020) The genetic risk for hypertension is lower among the Hungarian Roma population compared to the general population. PLoS ONE 15(6):e0234547
108. Fung MM, Nguyen C, Mehtani P, Salem RM, Perez B, Thomas B et al (2008) Genetic variation within adrenergic pathways determines in vivo effects of presynaptic stimulation in humans. Circulation 117(4):517–525
109. Thomsen LCV, McCarthy NS, Melton PE, Cadby G, Austgulen R, Nygård OK et al (2017) The antihypertensive MTHFR gene polymorphism rs17367504-G is a possible novel protective locus for preeclampsia. J Hypertens 35(1):132–139
110. Musso G, Saba F, Cassader M, Paschetta E, De Michieli F, Pinach S et al (2019) Angiotensin II type 1 receptor rs5186 gene variant predicts incident NAFLD and associated hypertension: role of dietary fat-induced pro-inflammatory cell activation. Am J Gastroenterol 114(4):607–619
111. Kundu A, Anand A (2013) Computational study of ADD1 gene polymorphism associated with hypertension. Cell Biochem Biophys 65(1):13–19
112. Ren M, Ng FL, Warren HR, Witkowska K, Baron M, Jia Z et al (2018) The biological impact of blood pressure-associated genetic variants in the natriuretic peptide receptor C gene on human vascular smooth muscle. Hum Mol Genet 27(1):199–210
113. Gamil S, Erdmann J, Abdalrahman IB, Mohamed AO (2017) Association of NOS3 gene polymorphisms with essential hypertension in Sudanese patients: a case control study. BMC Med Genet 18(1):128
114. Azam AB, Azizan EAB (2018) Brief overview of a decade of genome-wide association studies on primary hypertension. Int J Endocrinol 2018:7259704
115. Lardjam-Hetraf SA, Mediene-Benchekor S, Ouhaibi-Djellouli H, Meroufel DN, Boulenouar H, Hermant X et al (2015) Effects of established blood pressure loci on blood pressure values and hypertension risk in an Algerian population sample. J Hum Hypertens 29(5):296–302
116. Padmanabhan S, Melander O, Johnson T, Di Blasio AM, Lee WK, Gentilini D et al (2010) Genome-wide association study of blood pressure extremes identifies variant near UMOD associated with hypertension. PLoS Genet 6(10):e1001177
117. Hong GL, Chen XZ, Liu Y, Liu YH, Fu X, Lin SB et al (2013) Genetic variations in MOV10 and CACNB2 are associated with hypertension in a Chinese Han population. Genet Mol Res 12(4):6220–6227
118. Levy D, Ehret GB, Rice K, Verwoert GC, Launer LJ, Dehghan A et al (2009) Genome-wide association study of blood pressure and hypertension. Nat Genet 41(6):677–687
119. International Consortium for Blood Pressure Genome-Wide Association Studies, Ehret GB, Munroe PB, Rice KM, Bochud M, Johnson AD et al (2011) Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. Nature 478(7367):103–109
120. Chen Y-L, Li T-J, Hao Y, Wu B-G, Li H, Geng N et al (2018) Association of rs2271037 and rs3749585 polymorphisms in CORIN with susceptibility to hypertension in a Chinese Han population: a case-control study. Gene 20(651):79–85
121. Nossent AY, Hansen JL, Doggen C, Quax PHA, Sheikh SP, Rosendaal FR (2011) SNPs in microRNA binding sites in 3′-UTRs of RAAS genes influence arterial blood pressure and risk of myocardial infarction. Am J Hypertens 24(9):999–1006
122. Maher BS, Vladimirov VI, Latendresse SJ, Thiselton DL, McNamee R, Kang M et al (2011) The AVPR1A gene and substance use disorders: association, replication, and functional evidence. Biol Psychiatry 70(6):519–527
123. Fu X, Guo L, Jiang Z-M, Zhao L-S, Xu A-G (2014) An miR-143 promoter variant associated with essential hypertension. Int J Clin Exp Med 7(7):1813–1817
124. Hanin G, Shenhar-Tsarfaty S, Yayon N, Yau YH, Hoe YY, Bennett ER et al (2014) Competing targets of microRNA-608 affect anxiety and hypertension. Hum Mol Genet 23(17):4569–4580
125. Lin W-J, Salton SR (2013) The regulated secretory pathway and human disease: insights from gene variants and single nucleotide polymorphisms. Front Endocrinol 4:96
126. Kayima J, Liang J, Natanzon Y, Nankabirwa J, Ssinabulya I, Nakibuuka J et al (2017) Association of genetic variation with blood pressure traits among East Africans. Clin Genet 92(5):487–494
127. Zhang R, Witkowska K, Afonso Guerra-Assunção J, Ren M, Ng FL, Mauro C et al (2016) A blood pressure-associated variant of the SLC39A8 gene influences cellular cadmium accumulation and toxicity. Hum Mol Genet 25(18):4117–4126
128. Zhong L-L, Ding L-S, He W, Tian X-Y, Cao H, Song Y-Q et al (2017) Systolic hypertension related single nucleotide polymorphism is associated with susceptibility of ischemic stroke. Eur Rev Med Pharmacol Sci 21(12):2901–2906
129. Hong K-W, Jin H-S, Lim J-E, Kim S, Go MJ, Oh B (2010) Recapitulation of two genomewide association studies on blood pressure and essential hypertension in the Korean population. J Hum Genet 55(6):336–341
130. Lin Y, Lai X, Chen B, Xu Y, Huang B, Chen Z et al (2011) Genetic variations in CYP17A1, CACNB2 and PLEKHA7 are associated with blood pressure and/or hypertension in She ethnic minority of China. Atherosclerosis 219(2):709–714
131. Wahlstrand B, Orho-Melander M, Delling L, Kjeldsen S, Narkiewicz K, Almgren P et al (2009) The myocardial infarction associated CDKN2A/CDKN2B locus on chromosome 9p21 is associated with stroke independently of coronary events in patients with hypertension. J Hypertens 27(4):769–773
132. Newton-Cheh C, Larson MG, Vasan RS, Levy D, Bloch KD, Surti A et al (2009) Association of common variants in NPPA and NPPB with circulating natriuretic peptides and blood pressure. Nat Genet 41(3):348–353
133. Tabara Y, Kohara K, Kita Y, Hirawa N, Katsuya T, Ohkubo T et al (2010) Common variants in the ATP2B1 gene are associated with susceptibility to hypertension: the Japanese Millennium Genome Project. Hypertens Dallas Tex 56(5):973–980
134. Hong K-W, Jin H-S, Lim J-E, Cho YS, Go MJ, Jung J et al (2010) Non-synonymous single-nucleotide polymorphisms associated with blood pressure and hypertension. J Hum Hypertens 24(11):763–774
135. Hong K-W, Go MJ, Jin H-S, Lim J-E, Lee J-Y, Han BG et al (2010) Genetic variations in ATP2B1, CSK, ARSG and CSMD1 loci are related to blood pressure and/or hypertension in two Korean cohorts. J Hum Hypertens 24(6):367–372
136. Sun D, Zhou T, Heianza Y, Li X, Fan M, Fonseca VA et al (2019) Type 2 diabetes and hypertension. Circ Res 124(6):930–937

137. Qu Y-L, Wu C-M, Zhang L-X, Wen B-L, Zhang X, Ma C et al (2016) Association between alpha-adducin gene rs4963 polymorphism and hypertension risk in Asian population: a meta-analysis. Cell Mol Biol Noisy Gd Fr 62(13):62–64
138. Lu X, Wang L, Lin X, Huang J, Charles GC, He M et al (2015) Genome-wide association study in Chinese identifies novel loci for blood pressure and hypertension. Hum Mol Genet 24(3):865–874
139. Shen G-Q, Li L, Rao S, Abdullah KG, Ban JM, Lee B-S et al (2008) Four SNPs on chromosome 9p21 in a South Korean population implicate a genetic locus that confers high cross-race risk for development of coronary artery disease. Arterioscler Thromb Vasc Biol 28(2):360–365
140. Smith JG, Melander O, Lövkvist H, Hedblad B, Engström G, Nilsson P et al (2009) Common genetic variants on chromosome 9p21 confers risk of ischemic stroke: a large-scale genetic association study. Circ Cardiovasc Genet 2(2):159–164
141. Lin H-F, Tsai P-C, Lin R-T, Khor G-T, Sheu S-H, Juo S-HH (2010) Sex differential genetic effect of chromosome 9p21 on subclinical atherosclerosis. PLoS ONE 5(11):e15124
142. Siffert W, Forster P, Jöckel K-H, Mvere DA, Brinkmann B, Naber C et al (1999) Worldwide ethnic distribution of the G protein β3 subunit 825T allele and its association with obesity in Caucasian, Chinese, and Black African individuals. J Am Soc Nephrol 10(9):1921–1930
143. Stender S, Nordestgaard BG, Tybjaerg-Hansen A (2013) Elevated body mass index as a causal risk factor for symptomatic gallstone disease: a Mendelian randomization study. Hepatology 58(6):2133–2141
144. Zhao J, Bradfield JP, Li M, Wang K, Zhang H, Kim CE et al (2009) The role of obesity-associated loci identified in genome-wide association studies in the determination of pediatric BMI. Obesity 17(12):2254–2257
145. Wang Y, Zhang Y, Zhang J, Tang X, Qian Y, Gao P et al (2013) Association of a functional single-nucleotide polymorphism in the ALDH2 gene with essential hypertension depends on drinking behavior in a Chinese Han population. J Hum Hypertens 27(3):181–186
146. Hasi T, Hao L, Yang L, Su XL (2011) Acetaldehyde dehydrogenase 2 SNP rs671 and susceptibility to essential hypertension in Mongolians: a case control study. Genet Mol Res 10(1):537–543
147. Li Z-M, Kong C-Y, Sun K-Y, Wang L-S (2017) The ALDH2 gene rs671 polymorphism is not associated with essential hypertension. Clin Exp Hypertens 39(8):691–695
148. Niu W, Zhang Y, Ji K, Gu M, Gao P, Zhu D (2010) Confirmation of top polymorphisms in hypertension genome wide association study among Han Chinese. Clin Chim Acta 411(19–20):1491–1495
149. Abdullah A, Peeters A, de Courten M, Stoelwinder J (2010) The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract 89(3):309–319
150. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX et al (2006) Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease From the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 113(6):898–918
151. Lavie CJ, Milani RV, Ventura HO (2009) Obesity and cardiovascular disease. J Am Coll Cardiol 53(21):1925–1932
152. Sabia S, Kivimaki M, Shipley MJ, Marmot MG, Singh-Manoux A (2009) Body mass index over the adult life course and cognition in late midlife: the Whitehall II Cohort Study. Am J Clin Nutr 89(2):601–607
153. Ward MA, Carlsson CM, Trivedi MA, Sager MA, Johnson SC (2005) The effect of body mass index on global brain volume in middle-aged adults: a cross sectional study. BMC Neurol 5(1):23
154. Groen-Blokhuis MM, Franić S, van Beijsterveldt CEM, de Geus E, Bartels M, Davies GE et al (2013) A prospective study of the effects of breastfeeding and FADS2 polymorphisms on cognition and hyperactivity/attention problems. Am J Med Genet B Neuropsychiatr Genet 162(5):457–465
155. Hartwig FP, Davies NM, Horta BL, Victora CG, Davey Smith G (2016) Effect modification of *FADS2* polymorphisms on the association between breastfeeding and intelligence: protocol for a collaborative meta-analysis. BMJ Open 6(6):e010067
156. Ge L, Gordon JS, Hsuan C, Stenn K, Prouty SM (2003) Identification of the Δ-6 desaturase of human sebaceous glands: expression and enzyme activity. J Investig Dermatol 120(5):707–714
157. Stein DJ, Newman TK, Savitz J, Ramesar R (2006) Warriors versus worriers: the role of COMT gene variants. CNS Spectr 11(10):745–748
158. Ancín I, Cabranes JA, Vázquez-Álvarez B, Santos JL, Sánchez-Morla E, García-Jiménez MÁ et al (2011) Sensory gating deficit is associated with catechol-*O*-methyltransferase polymorphisms in bipolar disorder. World J Biol Psychiatry 12(5):376–384
159. Gupta M, Chauhan C, Bhatnagar P, Gupta S, Grover S, Singh PK et al (2009) Genetic susceptibility to schizophrenia: role of dopaminergic pathway gene polymorphisms. Pharmacogenomics 10(2):277–291
160. Prata DP, Mechelli A, Fu CHY, Picchioni M, Kane F, Kalidindi S et al (2009) Opposite effects of catechol-O-methyltransferase Val158Met on cortical function in healthy subjects and patients with schizophrenia. Biol Psychiatry 65(6):473–480
161. Shibata N, Nagata T, Tagai K, Shinagawa S, Ohnuma T, Kawai E et al (2015) Association between the catechol-O-methyltransferase polymorphism Val158Met and Alzheimer's disease in a Japanese population: COMT polymorphism and Alzheimer's disease. Int J Geriatr Psychiatry 30(9):927–933
162. Michaelovsky E, Gothelf D, Korostishevsky M, Frisch A, Burg M, Carmel M et al (2008) Association between a common haplotype in the COMT gene region and psychiatric disorders in individuals with 22q11.2DS. Int J Neuropsychopharmacol. https://doi.org/10.1017/S1461145707008085
163. Kring SII, Werge T, Holst C, Toubro S, Astrup A, Hansen T et al (2009) Polymorphisms of serotonin receptor 2A and 2C genes and COMT in relation to obesity and type 2 diabetes. PLoS ONE 4(8):e6696
164. CHARGE Cognitive Working Group, Marioni RE, Yang J, Dykiert D, Mõttus R, Campbell A et al (2016) Assessing the genetic overlap between BMI and cognitive function. Mol Psychiatry 21(10):1477–1482
165. Strachan MWJ, Reynolds RM, Marioni RE, Price JF (2011) Cognitive function, dementia and type 2 diabetes mellitus in the elderly. Nat Rev Endocrinol 7(2):108–114
166. Mõttus R, Luciano M, Starr JM, Deary IJ (2013) Diabetes and life-long cognitive ability. J Psychosom Res 75(3):275–278
167. Qizilbash N, Gregson J, Johnson ME, Pearce N, Douglas I, Wing K et al (2015) BMI and risk of dementia in two million people over two decades: a retrospective cohort study. Lancet Diabetes Endocrinol 3(6):431–436
168. Elias MF, Goodell AL, Dore GA (2012) Hypertension and cognitive functioning: a perspective in historical context. Hypertension 60(2):260–268
169. Sharma M, Kupferman JC, Brosgol Y, Paterno K, Goodman S, Prohovnik I et al (2010) The effects of hypertension on the paediatric brain: a justifiable concern. Lancet Neurol 9(9):933–940
170. Novak V, Hajjar I (2010) The relationship between blood pressure and cognitive function. Nat Rev Cardiol 7(12):686–698
171. Toth P, Tarantini S, Csiszar A, Ungvari Z (2017) Functional vascular contributions to cognitive impairment and dementia: mechanisms and consequences of cerebral autoregulatory dysfunction, endothelial impairment, and neurovascular uncoupling in aging. Am J Physiol-Heart Circ Physiol 312(1):H1-20
172. Chen Y-C, Liu Y-L, Tsai S-J, Kuo P-H, Huang S-S, Lee Y-S (2019) LRRTM4 and PCSK5 genetic polymorphisms as markers for cognitive impairment in a hypotensive aging population: a genome-wide association study in Taiwan. J Clin Med 8(8):1124
173. Cotman CW, Berchtold NC (2002) Exercise: a behavioral intervention to enhance brain health and plasticity. Trends Neurosci 25(6):295–301

Publisher's Note