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

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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
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 underling 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

\[
\text{IQ} = \frac{\text{mental age}}{\text{chronological age}} \times 100
\]

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 \(\text{Ca}^{2+}\) 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 \(\text{Mg}^{2+}\) ions and is highly expressed during brain and kidney development. rs7994356 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 ($p < 3.79 \times 10^{-8}$), LYLPLAL1 on chromosome 1 and rs10930502 ($p < 2.5 \times 10^{-7}$) METAP1D on chromosome 2 associated with BMI. The LYLPLAL1 (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 all variant alleles. These all 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 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, ($p < 9.08 \times 10^{-8}$), 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 chromosome 13; 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/disfunction. 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 adenylyl 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.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 ($p = 3 \times 10^{-8}$) 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,
| 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^{-11} | BP | 249,796 | GWAS | [26] |
| rs5443 | 12p13 | GNB3 | C>T | Enhanced G-protein activation | 000002 | 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 | Decline ability to elongate and desaturate fatty acid | 0018 | BMI, metabolic syndrome | 1037 | Candidate | [29] |
| rs1535 | 11q12.2 | FADS2 | A>G, T | Low BP | 4 × 10^{-5} | BMI, metabolic syndrome | 1037 | Candidate | [29, 30, 31] |
| rs17700633 | 18q21.3 | MC4R | G>A | Increased BMI | 001 | T2D | 14,940 | | [33] |
| rs1299548 | 7p21.3 | Near C1GALT1 | G>A, G>C | Visceral adipose tissue, BMI | 0039 | VAT | 2513 | GWAS | [34] |
| rs12517906 | 5q35.3 | LOC1002899003/MGAT1 | C>A, C>T | Fat absorption | 7.3 × 10^{-9} | 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 | 0001 | Obesity | 1152/1076/2249 | GWAS | [38] |
| rs1021001 | 5q35.3 | MGAT1 | C>G | Affect the level of serum unsaturated fatty acid | 0003 | Obesity | 1152/1076/2249 | GWAS | [38] |
| SNP name    | Chromosomal location | Gene          | Allele | Effect                                      | p value          | Associated trait                                         | Sample       | Method/study       | References |
|-------------|----------------------|---------------|--------|---------------------------------------------|------------------|----------------------------------------------------------|--------------|-------------------|------------|
| rs939584    | 2p25.3               | TMEM18        | C>G    | BMI at 20 years                             | $2.03 \times 10^{-5}$ | 11,586                                                   | GWAS         | [39]              |
| rs662799    | 11q23.3              | APOA5         | G>A    | Higher fasting triglyceride levels         | $2 \times 10^{-71}$ | 2280                                                     | HDL cholesterol, myocardial infarction | [40]    |
| rs13021737  | 2p25.3               | TMEM18        | A>C    | Increased BMI                              | 0.018            | 17,037                                                   | Obesity      | [41]              |
| rs1558902   | 16q12.2              | FTO           | T>A    | Maximum BMI                                | 0.037            | 1450                                                     | T2D, WC, obesity                       | [42]    |
| rs11191580  | 10q24.33             | NTSC2         | T>C    | Increased BMI                              | $3.83 \times 10^{-8}$ | Schizophrenia, bipolar disorder major depression     | 86,757/7488–47,354 |
| rs2535633   | 3p21.1               | ITIH4ITIH4-AS1| C>A    | Increased BMI                              | $1.77 \times 10^{-10}$ | 86,757/7488–47,354 | T2D          | [44]              |
| rs8050136   | 16q12.2              | FTO           | G>T    | Increased BMI                              | $4 \times 10^{-8}$ | 4189                                                     | T2D          | [45]              |
| rs12374818  | 7p                   | Near BBS9 and VAT |          | Increased BMI                              | $1.1 \times 10^{-7}$ | 2513                                                     | GWAS         | [34]              |
| rs3751812   | 16q12.2              | FTO           | G>T    | Increased BMI                              | $6 \times 10^{-10}$ | 2513                                                     | GWAS         | [46]              |
| rs18717449  | 16q12.2              | FTO           | G>T    | Increased BMI                              | $6 \times 10^{-10}$ | 2513                                                     | T2D          | [21, 46]         |
| rs10506943  | 12                   | CYCS3P30 and VAT-BMI |          | Increased BMI                              | $242 \times 10^{-7}$ | 2513                                                     | T2D          | [34]              |
| rs12186500  | 5q35.3               | MGAT1         | A>G    | Increased BMI                              | 0.001            | 1152/1076/2249                                           | GWAS         | [38]              |
| rs143665886 | 7q31.2               | LINCO1392     | T>C    | Increased BMI                              | $<0.0001$        | 3922                                                     | Diabetes hypertension              | [47]    |
| rs11642015  | 16q12.2              | FTO           | C>T    | High BMI                                   | 0.0001           | 1536                                                     | Diabetes obesity                   | [48]    |
| rs11583200  | 1p33                 | ELAVL4        | C>T    | Effect positive direction with BMI         | 0.0008           | 17,037                                                   | WC, percent body fat and upper arm circumference | [41]    |
| rs16858082  | 4p12                 | GNPDA2        | A>G    | Leptin level elevate                       | $3 \times 10^{-4}$ | 3506                                                     | Myocardial infarction, high-density lipoprotein cholesterol levels | [49]    |
| rs12229654  | 12q24.11             | CUX2          | T>G    | Myocardial infarction                      | $456 \times 10^{-9}$ | 86,757/7488–47,352 | Myocardial infarction, high-density lipoprotein cholesterol levels | [44]    |
| 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  | Deregulation lipid metabolism           | 0.0028      | T2D WC                                     | 7225     | [51]                  |             |
| rs261967       | 5q15                  | Near PCSK1   | A > C  | Pancreatic dysfunction                   | 8 × 10⁻¹³   | Obesity T2D appendicular lean mass         | 2215     | GWAS                  | [52]        |
| rs4776970      | 15q23                 | MAP2K5       | A > C  |                                      | 3 × 10⁻⁷    | WC, T2D, depressive disorder, schizophrenia, bipolar disorder | 1624     |                       |             |
| rs10913469     | 1q25.2                | CRYZL2P-SEC16B | T > C  |                                      | 0.0041      | WC                                          | 7225     | GWAS                  | [51]        |
| rs10938397     | 4p12                  | GNPDA2       | A > G  |                                      | 0.00093     | WC, 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 × 10⁻⁹    |                                      | 2813     |                       | [56]        |
| rs11142387     | 9q21.12               | KLF9         | A > T  | Higher BMI                              | 3.4 × 10⁻⁴  | Psychiatric disease, memory, performance   | 62,245/1624 | GWAS                  | [57]        |
| rs13130484     | 4p12                  | GNPDA2       | C > T  | 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]     |
| rs2207634      | 6p22.3                | CDKAL1       | C > G/T > T | Decreasing BMI                        | 1.4 × 10⁻¹¹ | T2D                                        | 62,245   | GWAS                  | [57]        |
| rs7138803      | 12q13.12              | FAIM2        | G > T/G > A | Increased BMI                        | 0.005       | WC, obesity, DBP                          | 3077/249796 | [54, 62]          |             |
| rs987237       | 6p12.3                | TFAP2B       | A > G  | Increased BMI                           | <5 × 10⁻⁸   | Obesity                                    | 249,796  | GWAS                  | [62]        |
| rs2241423      | 15q23                 | MAP2K5       | G > A  | Increased BMI                           | 0.0029      | 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                | TNIN3K       | C > T  | Increased BMI                           | 5.54 × 10⁻⁵ |                                      | 7225     | GWAS                  | [51]        |
| rs653178       | 1              | ATXN2        | C > G  | High BMI                                | 5 × 10⁻⁷    | DBP                                        | 2215     | GWAS                  | [56]        |
| rs12411886     | 10q24.32              | CNNM2Intron variant | C/A  | High BMI                                | 4 × 10⁻⁵    | CAD                                        | 1507     | 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                                  | 1507     |                       | [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 hemostasis      |          | PAGE                 | [20]       |
| rs2820436  | 1q41                 | LYPLAL1  | A/C    | High BMI  | <3.79 × 10⁻⁶ | 102,514                     |          | PAGE                 | [19]       |
| rs10930502 | 2q31.1               | METAP1D  | A/G    | High BMI  | <2.5 × 10⁻⁷ | 102,514                     |          | PAGE                 | [19]       |
| rs1934100  | 9p21.3               | ELAVL2   | A/T    | High BMI  | <5 × 10⁻⁸   | 200,452                     |          | GWAS                  | [19]       |
| rs754635   | 3p22.1               | CCK      | G/C    | High BMI  | <5 × 10⁻⁸   | 200,452                     |          | GWAS                  | [19]       |
| rs716527   | 15q25.2              | ZSCAN2   | C/T    | BMI-adjusted WC | <5 × 10⁻⁸ | WC                          | 200,452  | GWAS                  | [19]       |
| rs1720825  | 3q22.3               | MRAS     | A/G    | Increased BMI | 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              | MTF3     | G>A, G>C, G>T | Increased BMI | <5 × 10⁻⁸ | Obesity                      | 249,796  | [62]       |
| rs6265     | 11p14.1              | BNDF     | C>T    | Obesity hypertension short-term plasticity and learning | 1 × 10⁻¹⁴ | 3503                       | GWAS     | [39]       |
|           |                      |          |        |            |              |                             |          |                      |            |
| SNP name  | Chromosomal location | Gene      | Allele | Effect                                      | p value   | Associated trait                                      | Sample | Method/study | References |
|-----------|-----------------------|-----------|--------|---------------------------------------------|-----------|------------------------------------------------------|--------|--------------|------------|
| rs324650  | 7q33                  | CHRM2     | T > A  | PIQ-6.0                                     |           | Alcohol dependence and major depression              | 667    |              | [72]       |
| rs10457441| 6q16.1                | MIR2113   | T > A  | Decline in episodic memory                  | < 0.02    |                                                      | 1570   | GWAS         | [73]       |
| rs17522122| 14q12                 | AKAP6     | G > T  | Worse performance in episodic memory        | 4 × 10⁻⁹  | Working memory, Vocabulary and perceptual speed      | 1570   | GWAS         | [73]       |
| rs363039  | 20p12.2               | SNAP25    | G > A  | Highly associated with IQ variations        | < 0.01    |                                                      | 762    |              | [72]       |
| rs2721173 | 8q24.3                | LRR1C1    | C > T  |                                             | 9 × 10⁻⁶  |                                                      | 106,736/24,189 | GWAS | [74]       |
| rs11584700| 1q32.1                | 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 | GWAS | [74]       |
| rs4851266 | 2q11.2                | AFF3, LINCO1104 | C > T |                                             | 5 × 10⁻¹¹ |                                                      | 26 population | GWAS | [75]       |
| rs17518584| 3p12.1                | CADM2     | C > T  | Processing speed                             | 0.013     | T2D                                                  | 944    |              | [76]       |
| rs1487441 | 6q16.1                | LOC101927335, ALS89740.1 | G > A | Increased performance in cognitive domains and IQ | 2 × 10⁻⁹  |                                                      | 106,736/24,189 | GWAS | [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  | 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]       |
| SNP name | Chromosomal location | Gene | Allele | Effect | p value | Associated trait | Sample | Method/study | References |
|----------|----------------------|------|--------|--------|---------|------------------|--------|--------------|------------|
| rs1535   | 11q12.2              | FADS2| A & G  | 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 | Alzheimer’s disease cognitive impairment | Children-371 Adult-391 | [84]       |
| rs363016  | 20p12               | SNAP-25| C & T | Increased IQ | 0.0001 | Alzheimer’s disease cognitive impairment | Children-371 Adult-391 | [84]       |
| rs6265   | 11p14.1             | BDNF, BDNF-AS | C & T | Short-term learning |        | Obesity, Hypertension Schizophrenia | GWAS   |             | [85]       |
| rs2619539 | 6p22.3             | DTNBP1| C & A  | Increased verbal IQ (VIQ) | 0.005  | Alzheimer’s disease cognitive impairment | 232    | 793         | [86]       |
| rs362602  | 20p12-p11.2         | SNAP-25| A & G  | Increased IQ | < 0.01 | Alzheimer’s disease cognitive impairment | 682, 563 |             | [87]       |
| rs3758391 | 10q21.3             | SIRT1 | T & C  | Cardiovascular disease diabetes |        | GWAS |             | [88]       |
| rs11809911 | 1q23.3            | LMXA1| Associated with reduced IQ and memory/learning |        | 218   | GWAS |             | [79]       |
| rs9320913 | 6q16.1              | LOC1100129158 ALS89740.1 | C & A  | Associated with reduced IQ and memory/learning | 4.2 \times 10^{-9} | 101,069 | GWAS |             | [89]       |
| rs6948054 | 7q31-35             | CHRM2| A & G  | PIQ | 0.041  | 2158 |             | [78]       |
| rs8191992 | 7q31-35             | CHRM2| A & C  | PIQ | 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  | PIQ, full scale IQ (FSIQ) | 0.026  | 108|             | [77]       |
| rs324640  | 7q31-35             | CHRM2| G & A  | PIQ-5.2 | 0.667  | 667|             | [72]       |
| 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    | Strongly associated with intelligence | < 0.01   |                                                                   | 371,391 | [91]         |
| rs17800861    | 16p13.2              | GRIN2A| T>A    | 2.98 × 10⁻⁷                      |          | associated with general fluid cognitive function                               | 2,421   | [92]         |
| rs10119       | 19q13.32             | TOMM40| G>A    | 5.67 × 10⁻⁵                      |          |                                                                   | 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    | 8 × 10⁻⁹                         |          | Gene family PLEXIN member are mutated                                          | 1238    | GWAS         | [94]       |
| rs10794073    | 10q26.2              | ADAM12| A>C    | 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]       |
| rs1276583     | 6                    | RFPL4B| G/A/C/T| VIQ 7.13 × 10⁻⁷                  |          |                                                                   | 2421    | GWAS         | [92]       |
| rs12552228    | 9                    | TEK   | C>G    | 1.42 × 10⁻⁶                      |          |                                                                   | 2421    | GWAS         | [92]       |
| rs12554799    | 9                    | TEK   | C>G    | 8.51 × 10⁻⁷/PIQ-3 8 × 10⁻⁶       |          |                                                                   | 2421    | GWAS         | [92]       |
| rs705670      | 9q34.3               | LINC01502| C>G    | PIQ 3.09 × 10⁻⁷                  |          |                                                                   | 2421    | GWAS         | [92]       |
| rs4962520     | 10q26.2              | ADAM12| C>T    | 1.2 × 10⁻⁸                      |          | Associated with human longevity                                                | 1238    | GWAS         | [94]       |
| rs2490272     | 6q21                 | FOX 03| C/A/G/T| 9.96 × 10⁻¹⁴                     |          |                                                                   | 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]       |
| SNP name    | Chromosomal location | Gene            | Allele     | Effect                                      | p value          | Associated trait                                      | Sample     | Method/study | References |
|-------------|----------------------|-----------------|------------|---------------------------------------------|------------------|-----------------------------------------------------|------------|--------------|------------|
| rs66495454  | 1p31.1               | NEGR1           | TCC/TCCT   |                                             | $9.08 \times 10^{-9}$ | Diet measurement                                    | 54,119     | GWAS         | [69]       |
| rs113315451 | 20q13.13             | CSE1L Intron variant |           |                                             | $1.15 \times 10^{-8}$ |                                             | 54,119     | GWAS         | [69]       |
| rs236330    | 1                    | FNBP1L          | C > T      | Associated with IQ in adult and children    | $3.9 \times 10^{-15}$ |                                             | 17 989     | [68]         |
| rs1011313   | 6                    | DTNBPI          | 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                       | $2.84 \times 10^{-8}$ | FSIQ                                               | 65,866     | GWAS         | [69]       |
| rs411280    | 11q25                | NTM             | T > A/T > C|                                             | $< 10^{-3}$      | FSIQ                                               | 292 nuclear family | GWAS         | [71]       |
| rs3846329   | 4q31.23              | NR3C2           | G > C/G > T|                                             | $< 10^{-3}$      | FSIQ                                               | 292 nuclear family | GWAS         | [71]       |
| rs363050    | 20p12.2              | SNAP25          | G > A      |                                             | < 0.01           | VIQ                                                | 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-hypertension**

We discovered some SNPs that are actively participating in determination of BMI and BP [132]. Scientists examined through study of \(\sim 15,000\) Europeans that the rs5068 in NPPA gene is \(3’UTR\) region variant at 1p36.22 chromosome, is strongly associated \((p = 8 \times 10^{-76})\) 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),
| 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  | Diabetic nephropathy                                       | 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 | < 0.001 | Weight gain/decreased SBP                                | 165/6969    | [59–61]      |            |
| rs7138803 | 12q13.12             | FAIM2| G > T  | 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, BP, T2D                            | 38,759      | GWAS         | (102)      |
| rs17782313| 18                   | MC4R | T > A  | High BMI                             | < 0.05   | Weight gain/decreased SBP                                | 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  | 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/dangerous by having changes in the protein-coding region | 1.09 × 10^-6 | Heart disease, stroke                                    | 1113        | Candidate    | [111]      |
| rs11191580| 10q24.33             | NTSC2| 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]      |
| 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    | Reduced 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}      | Metabolic syndrome, arterial stiffness               | 1006        | GWAS              | [117]      |
| rs2681472      | 12q21.33             | ATP2B1                | A>G    | Elevate BP             | 7.1 × 10^{-6}    | CVD                                                  | 200,000     | GWAS              | [119]      |
| rs92764        | 10p23.33             | PLCE1                 | A>G    | Low density lipoprotein Cholesterol, higher risk of hypertension | 0.000002 | Obesity, Diabetes                                     | 808         | Candidate         | [28]       |
| rs5443         | 12p13                | GNB3                  | C>T    | Elevated G-protein activation | 0.029       | Obesity, Diabetes                                     |             | High-resolution melting (HRM) | [120]      |
| rs3749585      | 4p12                 | CORIN                 | A>G    | Reduction in miR-induced repression of gene expression, decreased BP | 0.009       | Myocardial infarction                                 |             | Dual luciferase reporter gene system | [121]      |
| rs13306046     | 19p13.3              | TBX12R                | C/T    | Reduced BP             | 0.001            | Decreased BP                                         | 350         | RT-PCR            | [50]       |
| rs10757274     | 9p21                 | CDKN2B-AS1            | A/G    | Elevate BP             | 0.001            | Weight gain                                           | 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       | Increased BP                                          | 350         | R-PCR             | [50]       |
| rs11174811     | 12q14-15             | AVPR1A                | C>A    | Increased BP           | 3 × 10^{-5}      | Myocardial infarction                                 | 343         | TaqMan assay      | [122]      |
| rs4705342      | 5q32                 | CARMN, MIR143         | T>C    | Associated with the risk of EH | 0.009       | Diabetes mellitus of ischemic stroke                 | 343         | TaqMan assay      | [123]      |
| rs71228616     | 7q22                 | ACHE, UFSP1           | G>T    | Minor allele shows elevated blood pressure | < 0.001  | Myocardial infarction                                 |             | GWAS              | [124]      |
| rs938671       | 17q21.2              | ATP6V0A1              | T>C    | Hypertension            | 0.003            | Hypertension risk                                     |             | GWAS              | [125]      |
| rs2681492      | 12q21.33             | ATP2B1                | A>G,G,G,G | SBP, DBP               | 3 × 10^{-11}     | CVD, diabetes                                         | 2881        | GWAS              | [126]      |
| rs8096897      | 18q21.2              | C18orf1               | SBP    | SBP                    | 3.2 × 10^{-11}   | CVD, diabetes                                         | 29,136      | GWAS              | [118]      |
| rs13107325     | 4p24                 | SLC39A8               | High BP | < 0.05 | BMI, intelligence                                   |             | GWAS              | [127]      |
| SNP name | Chromosomal location | Gene | Allele | Effect | p value | Associated trait | Sample size | Method/study | References |
|----------|----------------------|------|--------|--------|---------|------------------|------------|-------------|------------|
| rs3184504 | 12q24.12             | SH2B3 | T > A  | SBP    | 5 × 10⁻⁷ | Coronary heart disease, diabetes mellitus, BMI | 29,136     | GWAS        | [118]      |
| rs880315  | 1p36.22              | CASZ1 | T > C  | 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 B8 | A > G  | SBP    | 7.2 × 10⁻⁷ | Urinary albumin to creatinine ratio/ischemic stroke | 8512       | GWAS        | [129]      |
| rs11014166 | 10p12.31             | CACNB2 | A > T  | DBP/SBP| 8.7 × 10⁻⁷ | 8512                           | 29,136     | GWAS        | [129]      |
| rs1119154 | 10q24.3              | CYP17A1 | C > T  | SBP    | 0.002   | 8512                          | 29,136     | GWAS        | [130]      |
| rs11024074 | 11p15.2              | PLEKHA7 | T > C  | SBP    | 3.76 × 10⁻⁷ | 8512                           | 29,136     | GWAS        | [129]      |
| ra11105354 | 12q21.33             | ATP2B1 | A > G  | SBP    | 4 × 10⁻⁷  | Coronary heart disease, diabetes, myocardial infarction, stroke, obesity | 29,136     | GWAS        | [118]      |
| rs12579302 | 12q21.33             | ATP2B1 | A > G  | SBP    | 4 × 10⁻⁷  | Coronary heart disease, diabetes, myocardial infarction, stroke, obesity | 29,136     | GWAS        | [118]      |
| rs10757278 | 9p21.3               | CDK2A, CDK2B | A > GA > C A > T | Elevated BP | 1 × 10⁻²⁰ | Obesity, heart failure risk | 10,881     | RT-PCR      | [131, 50]  |
| rs5225    | 14q32.2              | BDKRB2 | T > A  | 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 × 10⁻¹⁰ | Obesity, heart failure risk | 14,743     | GWAS        | [132]      |
| rs1378942 | 15q24.1              | CSK    | C > A  | 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 | 29,136     | 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  | 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       | A/G/C  | Hypotension                      | 0.79    |                           | 38,970      |             | [65]       |
| rs2286672 | 17p13.2              | PLD2       | C/T    | Significantly decreased SBP     | 0.038   | Systemic Lupus Erythematosus | 8842        |             | [134]      |
| rs16935244| 1                    | AZIN2      | G > A  | Hypertension/DBP                 | 0.002   |                           | 8842        |             | [134]      |
| rs4963    | 4                    | ADD1       | C > G  | Hypertension                     | 0.001   |                           | 5097, 5937  |             | [137]      |
| rs2288774 | 18                   | NEDD4L     | CC- or CT | SBP                              | 0.01    |                           | 4001        |             | [103]      |
| rs4149601 | 18                   | NEDD4L     | G > A  | SBP                              | 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    | Hypertension                     | 0.0001  |                           | 752 hypertensive and 752 normotensive subjects |             | [104]      |
| rs4757391 | 11p15.2              | SOX6       | T > C  | DBP                              | $5 \times 10^{-9}$ |                           | 11,816      | GWAS        | [138]      |
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).

| 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 | Intronic variant |
| rs174575 | 11q12.2 | FADS2 | Intronic 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 | Intronic variant |
| rs5443 | 12p13 | GNB3 | Synonymous variant |
| rs9939609 | 16q12.2 | FTO | Intronic variant |
| rs17782313 | 18q21.3 | MCAR | Intronic variant |
| rs10938397 | 4p12 | GNPD2 | Intronic variant |
| rs671 | 12q24.12 | ALDH2 | Missense variant |
| rs7138803 | 12q13.2 | FAIM2 | Intronic variant |
| rs198358 | 1p36.22 | NPPA | 3’UTR region |
| rs653178 | 12q24.12 | ATXN2 | Intronic variant |
| rs11191580 | 10q24.33 | NT5C2 | Intronic 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 |

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
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. Val66Met 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. 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
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 rs62625 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; CV: 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; GxEn: Genotype–environmental interaction; HIP1: Huntingtin-interacting protein 1; HUFA: Highly unsaturated fatty acid; IQ: Intelligence quotient; MAP: Mean arterial pressure; PIQ: Performance intelligence quotient; PUFAs: Polyunsaturated fatty acids; 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.

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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.

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