



Angiotensin-Converting Enzyme Insertion/Deletion Gene Polymorphism (ACE I/D) in Egyptian Healthy Children and Adolescents

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
<i>ACE</i>	<i>Angiotensin converting enzyme</i>
<i>ACE2</i>	<i>Angiotensin II converting enzyme</i>
<i>ADAM17</i>	<i>A disintegrin and metalloproteinase 17</i>
<i>AgRP</i>	<i>Agouti-related peptide</i>
<i>AGT</i>	<i>Angiotensinogen</i>
<i>AGTR1</i>	<i>Angiotensinogen II type-1 receptor</i>
<i>AMPK</i>	<i>AMP-activated protein kinase</i>
<i>Ang I</i>	<i>Angiotensin I</i>
<i>Ang II</i>	<i>Angiotensin II</i>
<i>AP</i>	<i>Area postrema</i>
<i>ARBs</i>	<i>Angiotensin receptor blockers</i>
<i>ARC</i>	<i>Arcuate nucleus</i>
<i>AT1</i>	<i>Angiotensin 1</i>
<i>AT1R</i>	<i>Angiotensin II type 1 receptor</i>
<i>AT2R</i>	<i>Angiotensin type 2 receptor</i>
<i>AT7R</i>	<i>Angiotensin (1-7) receptor</i>
<i>ATII</i>	<i>Angiotensin II</i>
<i>BBB</i>	<i>Blood-brain barrier</i>
<i>BDNF</i>	<i>Brain-derived neurotrophic factor</i>
<i>BED</i>	<i>Binge eating disorder</i>
<i>BIA</i>	<i>Bioelectric Impedance Analysis</i>
<i>BK</i>	<i>Bradykinin</i>
<i>BMI</i>	<i>Body mass index</i>
<i>bp</i>	<i>Base pair</i>
<i>Bp</i>	<i>Blood pressure</i>
<i>CART</i>	<i>Cocaine- and amphetamine-regulated transcript</i>
<i>CCK</i>	<i>Cholecystokinin</i>
<i>CD</i>	<i>Collecting duct</i>
<i>CDC</i>	<i>Centers for Disease Control</i>
<i>CGH</i>	<i>Comparative genomic hybridization</i>
<i>cGMP</i>	<i>Cyclic guanosine monophosphate</i>
<i>COX-2</i>	<i>Cyclooxygenase-2</i>

List of Abbreviations cont...

Abb.	Full term
<i>CRH</i>	<i>Corticotrophin releasing hormone</i>
<i>CSF</i>	<i>Cerebro-spinal fluid</i>
<i>CT</i>	<i>Computed tomography</i>
<i>D₂ receptor</i>	<i>Dopamine receptor</i>
<i>DBP</i>	<i>Diastolic blood pressure</i>
<i>DMN</i>	<i>Dorsomedial nucleus</i>
<i>DNA</i>	<i>Deoxyribonucleic acid</i>
<i>DNA</i>	<i>Deoxyribonucleic acid</i>
<i>dNTP</i>	<i>Deoxy nucleotide triphosphate</i>
<i>DOHaD</i>	<i>Developmental origins of health and Disease</i>
<i>DVC</i>	<i>Dorsal vagal complex;</i>
<i>DXA</i>	<i>Dual-Energy X-ray Absorptiometry</i>
<i>EDTA</i>	<i>Ethylenediamine tetraacetic acid</i>
<i>EGFR</i>	<i>Epidermal growth factor receptor.</i>
<i>EP</i>	<i>E-prostanoid</i>
<i>ERK</i>	<i>Extracellular signal-regulated kinase</i>
<i>FFM</i>	<i>Fat free mass</i>
<i>gACE</i>	<i>Germinal angiotensin converting enzyme</i>
<i>GI</i>	<i>Gastrointestinal</i>
<i>GIT</i>	<i>Gastro intestinal tract</i>
<i>GLP-1</i>	<i>Glucagon-like peptide 1</i>
<i>HDL</i>	<i>High density lipoproteins</i>
<i>HEXXH</i>	<i>His-Glu-X-X-His</i>
<i>HOMA-IR</i>	<i>Homeostatic model assessment for</i>
<i>HWE</i>	<i>Hardy-Weinberg equilibrium</i>
<i>I/D</i>	<i>Insertion / deletion</i>
<i>IP 3</i>	<i>Inositol-1,4,5-triphosphate</i>
<i>IR</i>	<i>Insulin resistance</i>
<i>JAK2</i>	<i>Janus kinase 2</i>
<i>JG</i>	<i>Justaglomerular</i>
<i>Kb</i>	<i>Kilo bases</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>LD</i>	<i>Linkage disequilibrium</i>
<i>LDL</i>	<i>Low density lipoproteins</i>
<i>LHA</i>	<i>Lateral hypothalamic area</i>
<i>MAPKs</i>	<i>Mitogen-activated protein kinase serine</i>
<i>MC3R, MC4R</i>	<i>Melanocortin-3 and -4 receptor</i>
<i>MCH</i>	<i>Melanin concentrating hormone</i>
<i>mM</i>	<i>Master mix</i>
<i>mRG-D</i>	<i>Mas-related receptor</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>mRNA</i>	<i>Messenger RNA</i>
<i>NA</i>	<i>Nucleus accumbens</i>
<i>NAFLD</i>	<i>Nonalcoholic fatty liver disease</i>
<i>NEP</i>	<i>Neprilysin</i>
<i>NO</i>	<i>Nitric oxide</i>
<i>NPY</i>	<i>Neuropeptide Y</i>
<i>NTS</i>	<i>Nucleus of the solitary tract</i>
<i>ob -ob</i>	<i>Obese</i>
<i>Ob-R</i>	<i>Obesity receptor</i>
<i>Oxm</i>	<i>Oxyntomodulin</i>
<i>PCOS</i>	<i>Polycystic ovary syndrome</i>
<i>PCR</i>	<i>Polymerase chain reaction</i>
<i>PGE2</i>	<i>Prostaglandin E2</i>
<i>PKA</i>	<i>Protein kinase A</i>
<i>PKC</i>	<i>Protein kinase C</i>
<i>PLC</i>	<i>Phospholipase C</i>
<i>POMC</i>	<i>Pro-opiomelanocortin</i>
<i>POP</i>	<i>Prolyl oligopeptidase</i>
<i>PP</i>	<i>Pancreatic polypeptide</i>
<i>PPAR</i>	<i>Peroxisome proliferator-activated receptor</i>
<i>PPV</i>	<i>Positive Predictive value</i>
<i>PRR</i>	<i>Pro-renin receptor</i>
<i>PVN</i>	<i>Paraventricular nucleus</i>
<i>PYY</i>	<i>Peptide YY</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>RAS</i>	<i>Rennin-angiotensin system</i>
<i>ROC-curve</i>	<i>Receiver Operating Characteristic curve</i>
<i>ROS</i>	<i>Reactive oxygen species</i>
<i>ROS</i>	<i>Reactive oxygen species</i>
<i>sACE</i>	<i>Somatic angiotensin converting enzyme</i>
<i>SBP</i>	<i>Systolic blood pressure</i>
<i>SDS</i>	<i>Standard deviation score</i>
<i>SNP</i>	<i>Single-nucleotide polymorphism</i>
<i>STAT3</i>	<i>Signal transduction activated transcript 3</i>
<i>TBE</i>	<i>Borate buffer</i>
<i>TBE</i>	<i>Tris / Borate / EDTA</i>
<i>TBW</i>	<i>Total body water</i>
<i>TC</i>	<i>Total cholesterol</i>
<i>TOP</i>	<i>Thimet oligopeptidase</i>
<i>TRH</i>	<i>Thyroid releasing hormone</i>
<i>TV</i>	<i>Television</i>
<i>US</i>	<i>United State</i>
<i>VLDL</i>	<i>Very low density lipoproteins</i>
<i>VMN</i>	<i>Ventromedial nucleus</i>
<i>VSMC</i>	<i>Vascular smooth muscle cells</i>
<i>VTA</i>	<i>Ventral tegmental area</i>
<i>WAGR</i>	<i>Wilms tumor, aniridia, genitourinary anomaly, mental retardation</i>
<i>WC</i>	<i>Waist circumference</i>
<i>WHO</i>	<i>World Health organization</i>
<i>α-MSH</i>	<i>α-melanocyte-stimulating hormone</i>

INTRODUCTION

Overweight and obesity among children became an important public health concern as their prevalence within the pediatric population has been markedly increased in last decades (*Turudic, 2014*).

Currently, there is considerable interest in the genetics of complex human phenotypes such as obesity and hypertension.

The estimated heritability of adiposity measures range from 25–40% and several candidate genes have been identified for obesity phenotypes. The heritability of blood pressure phenotypes is estimated to be about 30% (*Eisenmann et al., 2009*).

The rennin-angiotensin system (RAS) is a complex multifaceted endocrine and paracrine system that mediates extracellular fluid and blood pressure homeostasis as well as a large variety of local physiological process at tissue level (*Fyhrquist and Saijonmaa, 2008*).

A widely prevalent insertion/ deletion (I/D) polymorphism in the ACE gene, characterized by the presence or absence of a 287-base-pair fragment, accounts for half of the variance in circulating levels of ACE, with II, ID and DD genotypes associated with lower, intermediate and higher plasma levels of the enzyme, respectively (*Lemes et al., 2013*).

The insertion/deletion polymorphism in the gene encoding the angiotensin-converting enzyme (ACE I/D) could be associated with arterial hypertension and obesity (*Patnaik et al., 2014*).

Angiotensin converting enzyme gene (ACE) is a possible candidate gene that may influence both body fatness and blood pressure. Although several genetic studies have been conducted in adults, relatively few studies have examined the potential candidate genes, and specifically ACE I/D, in healthy children (*Eisenmann et al., 2009*).