

Changes in the gene expression profile during spontaneous migraine attacks

Running head: RNA-sequencing of spontaneous migraine attacks

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Supplementary Materials

Table S1. Expression of migraine GWAS genes during and outside migraine attack.

Table S2. Enriched migraine-specific GO-terms.

Table S1. Expression of migraine GWAS genes during and outside migraine attack.

	<i>Migraine attack (A)</i>	<i>After treatment (B)</i>	<i>Outside attack (C)</i>	<i>After cold pressor test (D)</i>
<i>ADAMTSL4</i>	13385	13586	13196	14529
<i>ASTN2</i>	294	292	290	349
<i>CARF</i>	713	676	713	916
<i>CCM2L</i>	18	18	17	21
<i>CFDP1</i>	1476	1296	1332	1528
<i>DOCK4</i>	953	947	956	1107
<i>ECM1</i>	110	103	103	103
<i>HCK</i>	64250	59483	62189	62629
<i>HEY2</i>	18	15	19	16
<i>HJURP</i>	141	136	141	154
<i>HPSE2</i>	9	10	10	10
<i>HTRA1</i>	64	51	59	61
<i>IGSF9B</i>	416	411	452	497
<i>IMMP2L</i>	145	132	143	155
<i>ITPK1</i>	26348	24118	24951	24431
<i>JAG1</i>	232	252	255	301
<i>KCNK5</i>	85	81	91	86
<i>LRP1</i>	16558	14068	15993	15534
<i>MED14</i>	3278	3135	3227	3649
<i>MEF2D</i>	12061	11928	12267	12732
<i>MPPED2</i>	92	91	99	112
<i>NCOA7</i>	1632	1562	1637	1975
<i>NLRP1</i>	59740	57036	57938	62130
<i>NOTCH4</i>	531	456	517	523
<i>NRP1</i>	375	349	394	405
<i>PHACTR1</i>	1845	1978	1702	1877
<i>PLCE1</i>	581	588	607	725
<i>PRDM16</i>	38	38	40	44
<i>REST</i>	3182	3144	3213	3858
<i>RNF213</i>	80118	77507	81327	85673
<i>SLC24A3</i>	176	186	170	174
<i>SPINK2</i>	30	30	30	35
<i>STAT6</i>	86242	81865	84292	86766
<i>TGFBR2</i>	26516	26105	26301	30033
<i>TRPM8</i>	100	96	97	114
<i>TSPAN2</i>	1938	2027	1984	2466
<i>UFL1</i>	1286	1217	1282	1691
<i>USP9X</i>	10365	10203	9859	11268
<i>WSCD1</i>	12	11	12	12
<i>YAP1</i>	18	18	16	22
<i>ZCCHC14</i>	1297	1244	1298	1423

Table S2. Enriched migraine-specific GO-terms.

<i>Network Cluster*</i>	<i>cluster</i>	<i>GOterm**</i>	<i>process</i>	<i>adjP***</i>
A-0	0	GO:0000079	regulation of cyclin-dependent protein serine/threonine kinase activity	0.0148
A-0	0	GO:0006323	DNA packaging	0.00988
A-0	0	GO:0007018	microtubule-based movement	0.0332
A-0	0	GO:0007063	regulation of sister chromatid cohesion	0.0177
A-0	0	GO:0018105	peptidyl-serine phosphorylation	0.0305
A-0	0	GO:0030330	DNA damage response, signal transduction by p53 class mediator	0.0474
A-0	0	GO:0030890	positive regulation of B cell proliferation	0.0246
A-0	0	GO:0031571	mitotic G1 DNA damage checkpoint	0.0294
A-0	0	GO:0032466	negative regulation of cytokinesis	0.0294
A-0	0	GO:0042770	signal transduction in response to DNA damage	0.0102
A-0	0	GO:0044783	G1 DNA damage checkpoint	0.0294
A-0	0	GO:0044819	mitotic G1/S transition checkpoint	0.0294
A-0	0	GO:0045740	positive regulation of DNA replication	0.00203
A-0	0	GO:0048518	positive regulation of biological process	0.0102
A-0	0	GO:0050871	positive regulation of B cell activation	0.0474
A-0	0	GO:0051098	regulation of binding	0.0299
A-0	0	GO:0051302	regulation of cell division	0.0408
A-0	0	GO:0051782	negative regulation of cell division	0.0177
A-0	0	GO:0071158	positive regulation of cell cycle arrest	0.0299
A-0	0	GO:0071163	DNA replication preinitiation complex assembly	0.00458
A-0	0	GO:0072413	signal transduction involved in mitotic cell cycle checkpoint	0.0246
A-0	0	GO:0072431	signal transduction involved in mitotic G1 DNA damage checkpoint	0.0246
A-0	0	GO:0090329	regulation of DNA-dependent DNA replication	0.0019
A-0	0	GO:1902400	intracellular signal transduction involved in G1 DNA damage checkpoint	0.0246
A-0	0	GO:1902402	signal transduction involved in mitotic DNA damage checkpoint	0.0246
A-0	0	GO:1902403	signal transduction involved in mitotic DNA integrity checkpoint	0.0246
A-0	0	GO:1902806	regulation of cell cycle G1/S phase transition	0.0072
A-0	0	GO:1904029	regulation of cyclin-dependent protein kinase activity	0.0224
A-0	0	GO:1904668	positive regulation of ubiquitin protein ligase activity	0.0294
A-0	0	GO:2000045	regulation of G1/S transition of mitotic cell cycle	0.0135
A-0	0	GO:2000105	positive regulation of DNA-dependent DNA replication	0.000309
A-1	1	GO:0006266	DNA ligation	0.0146
A-1	1	GO:0017148	negative regulation of translation	0.0349
A-1	1	GO:0031124	mRNA 3'-end processing	0.0146
A-1	1	GO:0031392	regulation of prostaglandin biosynthetic process	0.0146

A-1	1	GO:0032069	regulation of nuclease activity	0.00411
A-1	1	GO:0035722	interleukin-12-mediated signaling pathway	0.0393
A-1	1	GO:0070671	response to interleukin-12	0.0467
A-1	1	GO:0071349	cellular response to interleukin-12	0.0467
A-1	1	GO:0090305	nucleic acid phosphodiester bond hydrolysis	0.0118
A-1	1	GO:2001279	regulation of unsaturated fatty acid biosynthetic process	0.0264
A-2	2	GO:0001819	positive regulation of cytokine production	0.0314
A-2	2	GO:0002281	macrophage activation involved in immune response	0.0212
A-2	2	GO:0008625	extrinsic apoptotic signaling pathway via death domain receptors	0.00974
A-2	2	GO:0019370	leukotriene biosynthetic process	0.0212
A-2	2	GO:0032102	negative regulation of response to external stimulus	0.0123
A-2	2	GO:0032271	regulation of protein polymerization	0.0314
A-2	2	GO:0032479	regulation of type I interferon production	0.0189
A-2	2	GO:0032648	regulation of interferon-beta production	0.00642
A-2	2	GO:0032649	regulation of interferon-gamma production	0.0367
A-2	2	GO:0032652	regulation of interleukin-1 production	0.0426
A-2	2	GO:0032677	regulation of interleukin-8 production	0.0468
A-2	2	GO:0032688	negative regulation of interferon-beta production	0.0212
A-2	2	GO:0070887	cellular response to chemical stimulus	0.0314
A-2	2	GO:0071345	cellular response to cytokine stimulus	0.0204
A-3	3	GO:0000186	activation of MAPKK activity	0.0399
A-3	3	GO:0002224	toll-like receptor signaling pathway	0.0177
A-3	3	GO:0002755	MyD88-dependent toll-like receptor signaling pathway	0.0114
A-3	3	GO:0007049	cell cycle	0.0149
A-3	3	GO:0007249	I-kappaB kinase/NF-kappaB signaling	0.0341
A-3	3	GO:0007257	activation of JUN kinase activity	0.0436
A-3	3	GO:0009892	negative regulation of metabolic process	0.0443
A-3	3	GO:0009893	positive regulation of metabolic process	0.0377
A-3	3	GO:0009896	positive regulation of catabolic process	0.0393
A-3	3	GO:0010556	regulation of macromolecule biosynthetic process	0.0207
A-3	3	GO:0010604	positive regulation of macromolecule metabolic process	0.0144
A-3	3	GO:0016579	protein deubiquitination	0.0406
A-3	3	GO:0019222	regulation of metabolic process	0.0335
A-3	3	GO:0030334	regulation of cell migration	0.0389
A-3	3	GO:0031058	positive regulation of histone modification	0.0304
A-3	3	GO:0031063	regulation of histone deacetylation	0.021
A-3	3	GO:0031065	positive regulation of histone deacetylation	0.0145
A-3	3	GO:0031323	regulation of cellular metabolic process	0.00704
A-3	3	GO:0031324	negative regulation of cellular metabolic process	0.0335
A-3	3	GO:0031325	positive regulation of cellular metabolic process	0.0287
A-3	3	GO:0031326	regulation of cellular biosynthetic process	0.0177
A-3	3	GO:0031399	regulation of protein modification process	0.0287

A-3	3	GO:0031401	positive regulation of protein modification process	0.0393
A-3	3	GO:0032268	regulation of cellular protein metabolic process	0.0281
A-3	3	GO:0033554	cellular response to stress	0.0399
A-3	3	GO:0035556	intracellular signal transduction	0.0389
A-3	3	GO:0038089	positive regulation of cell migration by vascular endothelial growth factor signaling pathway	0.0393
A-3	3	GO:0042176	regulation of protein catabolic process	0.0324
A-3	3	GO:0044264	cellular polysaccharide metabolic process	0.0399
A-3	3	GO:0045732	positive regulation of protein catabolic process	0.0346
A-3	3	GO:0048523	negative regulation of cellular process	0.0315
A-3	3	GO:0051128	regulation of cellular component organization	0.021
A-3	3	GO:0051171	regulation of nitrogen compound metabolic process	0.0065
A-3	3	GO:0051173	positive regulation of nitrogen compound metabolic process	0.0177
A-3	3	GO:0051270	regulation of cellular component movement	0.0242
A-3	3	GO:0051338	regulation of transferase activity	0.0287
A-3	3	GO:0060255	regulation of macromolecule metabolic process	0.0106
A-3	3	GO:0061136	regulation of proteasomal protein catabolic process	0.00915
A-3	3	GO:0080135	regulation of cellular response to stress	0.021
A-3	3	GO:0090045	positive regulation of deacetylase activity	0.0242
A-3	3	GO:0090312	positive regulation of protein deacetylation	0.021
A-3	3	GO:0150065	regulation of deacetylase activity	0.0242
A-3	3	GO:1901673	regulation of mitotic spindle assembly	0.0348
A-3	3	GO:1901699	cellular response to nitrogen compound	0.0315
A-3	3	GO:1901725	regulation of histone deacetylase activity	0.0242
A-3	3	GO:1901727	positive regulation of histone deacetylase activity	0.0242
A-3	3	GO:1901800	positive regulation of proteasomal protein catabolic process	0.0335
A-3	3	GO:1903362	regulation of cellular protein catabolic process	0.0389
A-3	3	GO:2000112	regulation of cellular macromolecule biosynthetic process	0.0287
A-3	3	GO:2000145	regulation of cell motility	0.0214
A-4	4	GO:0070527	platelet aggregation	0.043
A-9	9	GO:0003002	regionalization	0.0359
A-9	9	GO:0003008	system process	0.0233
A-9	9	GO:0021513	spinal cord dorsal/ventral patterning	0.0374
A-9	9	GO:0030325	adrenal gland development	0.0339
A-9	9	GO:0050877	nervous system process	0.0145
A-9	9	GO:0050906	detection of stimulus involved in sensory perception	0.033
A-10	10	GO:0006511	ubiquitin-dependent protein catabolic process	0.0405
A-10	10	GO:0019941	modification-dependent protein catabolic process	0.0432
A-10	10	GO:0043161	proteasome-mediated ubiquitin-dependent protein catabolic process	0.016
A-10	10	GO:0043412	macromolecule modification	0.0298
A-10	10	GO:0043632	modification-dependent macromolecule catabolic process	0.0462

A-10	10	GO:0051603	proteolysis involved in cellular protein catabolic process	0.0392
A-12	12	GO:0001932	regulation of protein phosphorylation	0.0444
A-12	12	GO:0002698	negative regulation of immune effector process	0.0186
A-12	12	GO:0002920	regulation of humoral immune response	0.0354
A-12	12	GO:0003013	circulatory system process	0.0302
A-12	12	GO:0007154	cell communication	0.0243
A-12	12	GO:0007165	signal transduction	0.0369
A-12	12	GO:0007166	cell surface receptor signaling pathway	0.00329
A-12	12	GO:0008015	blood circulation	0.0254
A-12	12	GO:0009967	positive regulation of signal transduction	0.0186
A-12	12	GO:0023052	signaling	0.0398
A-12	12	GO:0031348	negative regulation of defense response	0.00161
A-12	12	GO:0033993	response to lipid	0.0428
A-12	12	GO:0034367	protein-containing complex remodeling	0.00412
A-12	12	GO:0034368	protein-lipid complex remodeling	0.00412
A-12	12	GO:0034369	plasma lipoprotein particle remodeling	0.00412
A-12	12	GO:0034370	triglyceride-rich lipoprotein particle remodeling	0.00959
A-12	12	GO:0034372	very-low-density lipoprotein particle remodeling	0.00419
A-12	12	GO:0045926	negative regulation of growth	0.0159
A-12	12	GO:0050790	regulation of catalytic activity	0.0385
A-12	12	GO:0050900	leukocyte migration	0.0263
A-12	12	GO:0051239	regulation of multicellular organismal process	0.0475
A-12	12	GO:0051241	negative regulation of multicellular organismal process	0.00863
A-12	12	GO:0051336	regulation of hydrolase activity	0.0126
A-12	12	GO:0051716	cellular response to stimulus	0.0339
A-12	12	GO:0071825	protein-lipid complex subunit organization	0.0143
A-12	12	GO:0071827	plasma lipoprotein particle organization	0.0119
A-13	13	GO:0006811	ion transport	0.00506
A-13	13	GO:0006812	cation transport	0.00394
A-13	13	GO:0034220	ion transmembrane transport	0.00183
A-13	13	GO:0098655	cation transmembrane transport	0.0237
A-13	13	GO:0098660	inorganic ion transmembrane transport	0.00853
A-14	14	GO:0002475	antigen processing and presentation via MHC class Ib	0.0364
A-14	14	GO:0006783	heme biosynthetic process	0.0301
A-14	14	GO:0010506	regulation of autophagy	0.036
A-14	14	GO:0019724	B cell mediated immunity	0.0418
A-14	14	GO:0030097	hemopoiesis	0.0205
A-14	14	GO:0042592	homeostatic process	0.0192
A-14	14	GO:0048518	positive regulation of biological process	0.0299
A-14	14	GO:0048534	hematopoietic or lymphoid organ development	0.036
A-14	14	GO:0048878	chemical homeostasis	0.036
A-14	14	GO:0050896	response to stimulus	0.016
A-16	16	GO:0010035	response to inorganic substance	0.0304
A-16	16	GO:0010038	response to metal ion	0.0497

A-16	16	GO:0051249	regulation of lymphocyte activation	0.049
A-17	17	GO:0001655	urogenital system development	0.0431
A-17	17	GO:0072001	renal system development	0.045
A-19	19	GO:0006464	cellular protein modification process	0.0435
A-19	19	GO:0006879	cellular iron ion homeostasis	0.0286
A-19	19	GO:0036211	protein modification process	0.0435
A-19	19	GO:0045638	negative regulation of myeloid cell differentiation	0.0344
B-0	0	GO:0033260	nuclear DNA replication	0.0105
B-0	0	GO:0035088	establishment or maintenance of apical/basal cell polarity	0.0474
B-0	0	GO:0042074	cell migration involved in gastrulation	0.0105
B-0	0	GO:0044786	cell cycle DNA replication	0.0105
B-0	0	GO:0051307	meiotic chromosome separation	0.0172
B-0	0	GO:0061245	establishment or maintenance of bipolar cell polarity	0.0474
B-1	1	GO:0000209	protein polyubiquitination	0.00132
B-1	1	GO:0002220	innate immune response activating cell surface receptor signaling pathway	0.03
B-1	1	GO:0002283	neutrophil activation involved in immune response	0.0491
B-1	1	GO:0002478	antigen processing and presentation of exogenous peptide antigen	0.0218
B-1	1	GO:0006511	ubiquitin-dependent protein catabolic process	0.0292
B-1	1	GO:0010498	proteasomal protein catabolic process	0.024
B-1	1	GO:0019884	antigen processing and presentation of exogenous antigen	0.03
B-1	1	GO:0019941	modification-dependent protein catabolic process	0.0301
B-1	1	GO:0033209	tumor necrosis factor-mediated signaling pathway	0.0216
B-1	1	GO:0035567	non-canonical Wnt signaling pathway	0.0485
B-1	1	GO:0043161	proteasome-mediated ubiquitin-dependent protein catabolic process	0.0127
B-1	1	GO:0043312	neutrophil degranulation	0.047
B-1	1	GO:0043632	modification-dependent macromolecule catabolic process	0.0319
B-1	1	GO:0048002	antigen processing and presentation of peptide antigen	0.0347
B-1	1	GO:0051603	proteolysis involved in cellular protein catabolic process	0.0395
B-1	1	GO:0051973	positive regulation of telomerase activity	0.0485
B-1	1	GO:0071824	protein-DNA complex subunit organization	0.0485
B-1	1	GO:0090090	negative regulation of canonical Wnt signaling pathway	0.0496
B-1	1	GO:1901987	regulation of cell cycle phase transition	0.0142
B-1	1	GO:1901990	regulation of mitotic cell cycle phase transition	0.0445
B-1	1	GO:2000736	regulation of stem cell differentiation	0.0202
B-2	2	GO:0006333	chromatin assembly or disassembly	0.0157
B-2	2	GO:0006334	nucleosome assembly	0.0168
B-2	2	GO:0009611	response to wounding	0.00663
B-2	2	GO:0030041	actin filament polymerization	0.0344
B-2	2	GO:0031497	chromatin assembly	0.0318

<i>B-2</i>	2	GO:0034728	nucleosome organization	0.0168
<i>B-2</i>	2	GO:0043313	regulation of neutrophil degranulation	0.0169
<i>B-2</i>	2	GO:0043933	protein-containing complex subunit organization	0.00292
<i>B-2</i>	2	GO:0051345	positive regulation of hydrolase activity	0.0327
<i>B-2</i>	2	GO:0051651	maintenance of location in cell	0.0225
<i>B-2</i>	2	GO:0065003	protein-containing complex assembly	0.00503
<i>B-2</i>	2	GO:0065004	protein-DNA complex assembly	0.0268
<i>B-2</i>	2	GO:0071824	protein-DNA complex subunit organization	0.0269
<i>B-2</i>	2	GO:0090200	positive regulation of release of cytochrome c from mitochondria	0.0277
<i>B-2</i>	2	GO:0097435	supramolecular fiber organization	0.0426
<i>B-2</i>	2	GO:2001235	positive regulation of apoptotic signaling pathway	0.0344
<i>B-2</i>	2	GO:2001242	regulation of intrinsic apoptotic signaling pathway	0.0104
<i>B-2</i>	2	GO:2001243	negative regulation of intrinsic apoptotic signaling pathway	0.0426
<i>B-3</i>	3	GO:0006643	membrane lipid metabolic process	0.0336
<i>B-3</i>	3	GO:0008610	lipid biosynthetic process	0.0423
<i>B-4</i>	4	GO:0006950	response to stress	0.00445
<i>B-9</i>	9	GO:0001708	cell fate specification	0.0313
<i>B-9</i>	9	GO:0003156	regulation of animal organ formation	0.0356
<i>B-9</i>	9	GO:0009653	anatomical structure morphogenesis	0.0444
<i>B-9</i>	9	GO:0009887	animal organ morphogenesis	0.0464
<i>B-9</i>	9	GO:0021536	diencephalon development	0.029
<i>B-9</i>	9	GO:0022612	gland morphogenesis	0.014
<i>B-9</i>	9	GO:0030154	cell differentiation	0.04
<i>B-9</i>	9	GO:0030539	male genitalia development	0.029
<i>B-9</i>	9	GO:0030850	prostate gland development	0.0464
<i>B-9</i>	9	GO:0048468	cell development	0.0256
<i>B-9</i>	9	GO:0048598	embryonic morphogenesis	0.0356
<i>B-9</i>	9	GO:0048646	anatomical structure formation involved in morphogenesis	0.0464
<i>B-9</i>	9	GO:0048665	neuron fate specification	0.014
<i>B-9</i>	9	GO:0048732	gland development	0.0225
<i>B-9</i>	9	GO:0048736	appendage development	0.0444
<i>B-9</i>	9	GO:0048806	genitalia development	0.0178
<i>B-9</i>	9	GO:0048863	stem cell differentiation	0.0356
<i>B-9</i>	9	GO:0048869	cellular developmental process	0.0444
<i>B-9</i>	9	GO:0060173	limb development	0.0444
<i>B-9</i>	9	GO:0060571	morphogenesis of an epithelial fold	0.0319
<i>B-9</i>	9	GO:2000036	regulation of stem cell population maintenance	0.0356
<i>B-10</i>	10	GO:0036092	phosphatidylinositol-3-phosphate biosynthetic process	0.021
<i>B-11</i>	11	GO:0070098	chemokine-mediated signaling pathway	0.0306
<i>B-11</i>	11	GO:0140131	positive regulation of lymphocyte chemotaxis	0.0143
<i>B-11</i>	11	GO:1990868	response to chemokine	0.0399
<i>B-11</i>	11	GO:1990869	cellular response to chemokine	0.0399

<i>B-11</i>	11	GO:2000503	positive regulation of natural killer cell chemotaxis	0.00757
<i>B-12</i>	12	GO:0022617	extracellular matrix disassembly	0.0412
<i>B-12</i>	12	GO:0061025	membrane fusion	0.00803
<i>B-13</i>	13	GO:0001508	action potential	0.0124
<i>B-13</i>	13	GO:0009698	phenylpropanoid metabolic process	0.0153
<i>B-13</i>	13	GO:0009804	coumarin metabolic process	0.0153
<i>B-14</i>	14	GO:0002479	antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent	0.0304
<i>B-14</i>	14	GO:0006897	endocytosis	0.0357
<i>B-14</i>	14	GO:0034383	low-density lipoprotein particle clearance	0.00807
<i>B-14</i>	14	GO:0043277	apoptotic cell clearance	0.0485
<i>B-14</i>	14	GO:1901685	glutathione derivative metabolic process	0.0493
<i>B-14</i>	14	GO:1901687	glutathione derivative biosynthetic process	0.0493
<i>B-16</i>	16	GO:0097428	protein maturation by iron-sulfur cluster transfer	0.00624
<i>B-16</i>	16	GO:1903578	regulation of ATP metabolic process	0.0371
<i>B-17</i>	17	GO:0019752	carboxylic acid metabolic process	0.0323
<i>B-17</i>	17	GO:0042537	benzene-containing compound metabolic process	0.00297
<i>B-17</i>	17	GO:0048519	negative regulation of biological process	0.0462
<i>B-17</i>	17	GO:0072676	lymphocyte migration	0.0384
<i>B-19</i>	19	GO:0002221	pattern recognition receptor signaling pathway	0.00767
<i>B-19</i>	19	GO:0002755	MyD88-dependent toll-like receptor signaling pathway	0.0421
<i>B-19</i>	19	GO:0006954	inflammatory response	0.0232
<i>B-19</i>	19	GO:0007249	I-kappaB kinase/NF-kappaB signaling	0.0439
<i>B-19</i>	19	GO:0009617	response to bacterium	0.0343
<i>B-19</i>	19	GO:0016458	gene silencing	0.0439
<i>B-19</i>	19	GO:0032728	positive regulation of interferon-beta production	0.0419
<i>B-19</i>	19	GO:1901222	regulation of NIK/NF-kappaB signaling	0.0368
<i>B-19</i>	19	GO:1904645	response to amyloid-beta	0.0421
<i>B-19</i>	19	GO:1904646	cellular response to amyloid-beta	0.0214

*Clusters are marked with A and B, representing the networks ‘during migraine attack’ (A) and ‘after treatment’ (B).

**GOterm = Gene Ontology term

***P_{adj} = P-value adjusted for multiple-testing