Investigating migraine and mood disorder comorbidity in a community-based pediatric sample

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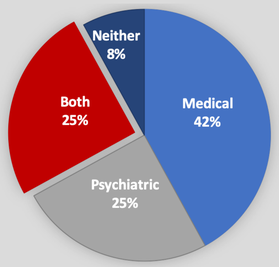
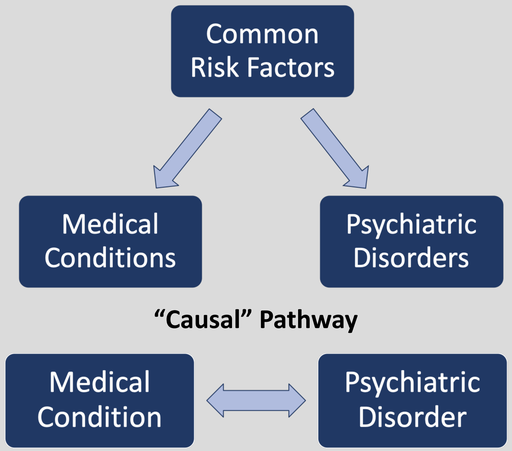
Background



> 50% of individuals with a psychiatric disorder also suffer from a chronic medical condition, which leads to:
- ↑ mortality
- ↑ health care costs
- ↑ functional impairment
- ↓ treatment response

Is there common genetic susceptibility to comorbid medical and mental disorders?

Common Etiology



"Causal" Pathway

Migraine/Mood

- Rates of psychiatric symptoms and disorders are elevated among youth with headache and migraine.
- Youths with migraine and comorbid conditions exhibit more general impairment, school absences, and greater continuity of headache over time.
- Twin and family studies have shown bidirectional relationships between migraine and depression.
- To date, no genes have been shown to be associated with both disorders.

Lifetime Disorder Prevalence

Disorder	N	Total %	Female %
Migraine	502	9.71	60.96
Depression	505	9.76	65.74
Mania	54	1.06	61.11
Bipolar Disorder	31	0.61	61.29
Total	5211		49.24

Migraine/Mood Associations

	Crude				Adjusted			
Migraine	Odds Ratio	95% CI		p-value	Odds Ratio	95% CI		p-value
Depression	2.37	1.84	3.02	<0.001	1.69	1.30	2.17	<0.001
Mania	3.29	1.72	5.95	<0.001	2.55	1.31	4.66	<0.001
Bipolar Disorder	3.83	1.66	8.09	<0.001	2.80	1.19	6.03	<0.01

Polygenic Risk Score/Disorder Associations

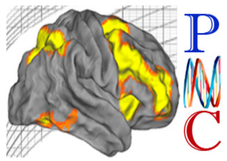
			Adjusted		
Score	Disorder	Odds Ratio	95% CI		p-value
Migraine	Migraine	1.16	1.06	1.27	<0.001
Depression	Depression	1.28	1.17	1.40	<0.001
Bipolar	Mania	1.03	0.73	1.44	ns
Bipolar	Bipolar	1.06	0.68	1.67	ns

Cross-Disorder Polygenic Risk Score Associations

			Adjusted		
Score	Disorder	Odds Ratio	95% CI		p-value
Migraine	Depression	0.93	0.85	1.02	ns
Migraine	Mania	0.95	0.73	1.24	ns
Migraine	Bipolar	1.10	0.78	1.54	ns
Depression	Migraine	1.09	1.00	1.19	ns

Methods

Sample: 5175 European-ancestry youth from the Philadelphia Neurodevelopmental Cohort (PNC), sampled from pediatric clinics in the greater Philadelphia area through the Children's Hospital of Philadelphia (CHOP)
Age: 8 to 21 years, mean 14.2 years; Sex: 51.7% female



Measures:
- Comprehensive screening interview for mental disorders
- Chronic physical conditions reported by parent and/or youth
- Electronic medical record review

Genotyping: Illumina SNP arrays, imputed on the Michigan Imputation Server, cleaned using a standard approach, hard calls generated in Plink (R^2>0.7, MAF>0.01)

Polygenic Risk Scores (PRS): **C**alculated using PRS-CS software package (https://github.com/getian107/PRScs) and summary data from publicly available GWAS controlling for 10 principal components of ancestry for Migraine, Depression, and Bipolar Disorder

Statistical Analysis: Patterns of migraine/mood comorbidity were established with logistic regression, adjusted for the participant's age and sex. Models with PRS predicting migraine or mood disorder were also performed, and adjusted for the participant's age and sex. All analyses were completed in the R statistical package.

Discussion

Migraine/Mood Comorbidity
- ✓ Strong associations between migraine and depression, mania, and bipolar disorder.
- ✓ Polygenic risk for migraine and depression from adult discovery samples were confirmed in youth, but were not significantly associated with comorbid disorders.
- ✓ Prospective tracking of cross-disorder comorbidity may provide insight into potential explanations and could inform prevention and intervention efforts.

Limitations
- Cross sectional - order of onset cannot be determined from these data
- Lack of control for comorbidity in PRS

Implications
- Prospective tracking of cross-disorder morbidity will be important to establish more effective mechanisms for prevention and intervention

Future Directions
- Derive empirically based subgroups of co-occurring disorders and their correlates

Acknowledgements

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