

# NF Family Day: Headache



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**Disclosures:**  
None

# Objectives

- Provide background on headaches
- Discuss headache classifications and symptoms
- Review neurofibromatosis headache epidemiology
- Review headache pathophysiology
- Discuss indications for diagnostic testing in pediatric headache disorders
- Discuss evidence based strategies for management in pediatric headache disorders

# Headache: Overall Impact

- The most common neurologic disorder in the general population
  - Curr Probl Pediatr Adolesc Health Care. 2017 Mar;47(3):44-65.
- Migraine is the 19<sup>th</sup> leading cause of years lived with disability
  - Am J Med Genet A. 2015 Oct;167A(10):2282-5.
- By 15 years old, 57-82% of children will have had a headache of any type
  - Curr Opin Pediatr. 2018 Dec;30(6):748-754
- From 15-25 years old, migraine prevalence as high as 28%
  - Curr Opin Pediatr. 2018 Dec;30(6):748-754.



# Primary vs. Secondary Headaches

- Primary Headaches

- Migraine
- Tension Type Headaches
- Trigeminal Autonomic Cephalalgia (TAC)

- Secondary Headaches

- Tumors
- Hydrocephalus
- Cerebrovascular
- Infectious
- Medication side effect



# Migraine

## Major Criteria

1. Headache duration: 2-72 hrs
2. At least 2 of the following
  - a. Bilateral or unilateral location
  - b. Pulsating quality
  - c. Moderate or severe pain
  - d. Aggravation by or causing avoidance of routine physical activity

## Minor Criteria

1. At least one of the following
  - a. Nausea and/or vomiting
  - b. Light and noise sensitivity

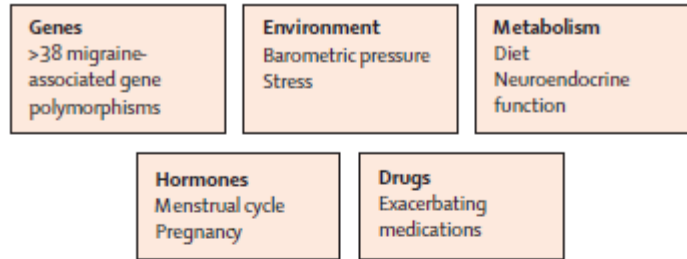


# Pathophysiology of Primary Headaches – A Perfect Storm of Stressors

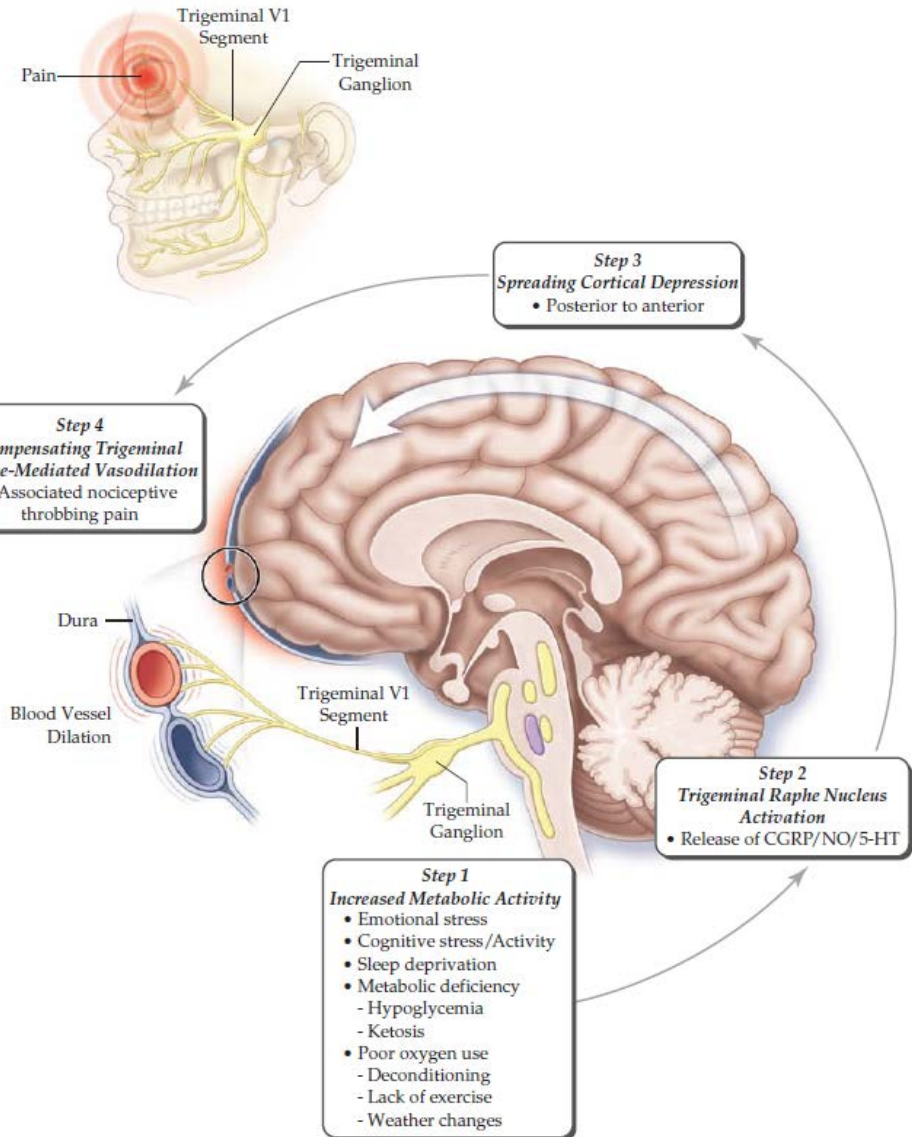
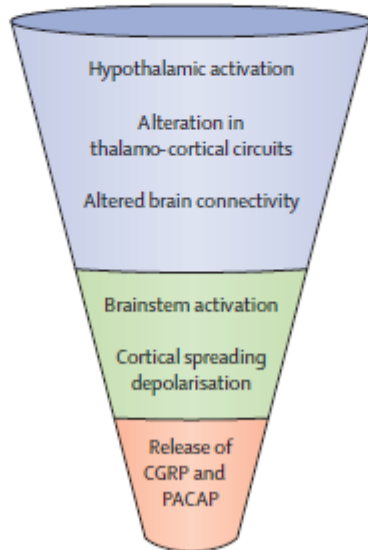
DiSabella M, Langdon R. Pediatric Headache Disorders. Scientific American Neurology; April 2017

Lancet Neurol 2018; 17: 174–82

## Factors



## Mechanisms



PACAP = Pituitary adenylate cyclase-activating polypeptide  
 CGRP = Calcitonin gene related peptide

# Tension Type Headache

## Major Criteria

1. Duration: 30 minutes - 7 days
2. At least 2 of the following:
  - a. Bilateral location
  - b. Pressing or tightening
  - c. Mild or moderate intensity
  - d. No aggravated by routine physical activity

## Minor Criteria

- Both of the following
- a. No nausea or vomiting
  - b. No more than one of photophobia or phonophobia



# Headache Compared to other Neurologic Complications of NF1

- 2018 Questionnaire - Japan
  - Intellectual Problems: 42.9%
  - Epilepsy: 13.8%
  - Optic Nerve glioma: 7.6%
    - Other brain tumor: 3.4%
  - ADHD: 40.2%
    - Only used parent report, so actual number likely lower
  - Headache: 49.6%
    - Migraine/suspected migraine: 31/123 (lower age range)
  - Cerebrovascular disease: 4.1%
  - Hydrocephalus: 1.4%
    - Pediatr Int. 2018 Jan;60(1):70-75
- 2020 Review Article
  - Headache in 34-65%
  - Hydrocephalus 1-5%
  - Cerebrovascular disease 2.5-6%
  - Polyneuropathy 1.3-2.3%
  - Epilepsy 4.2-14%
    - Neurol Sci. 2020 May 1. doi: 10.1007/s10072-020-04400-x. Online ahead of print.



# Are Headaches Different in People With Neurofibromatosis Type 1?



# Early Studies on Headache in NF1

Clementi M, Battistella PA, Rizzi L, Boni S, Tenconi R. Headache in patients with neurofibromatosis type 1. *Headache*. 1996;36(1):10.

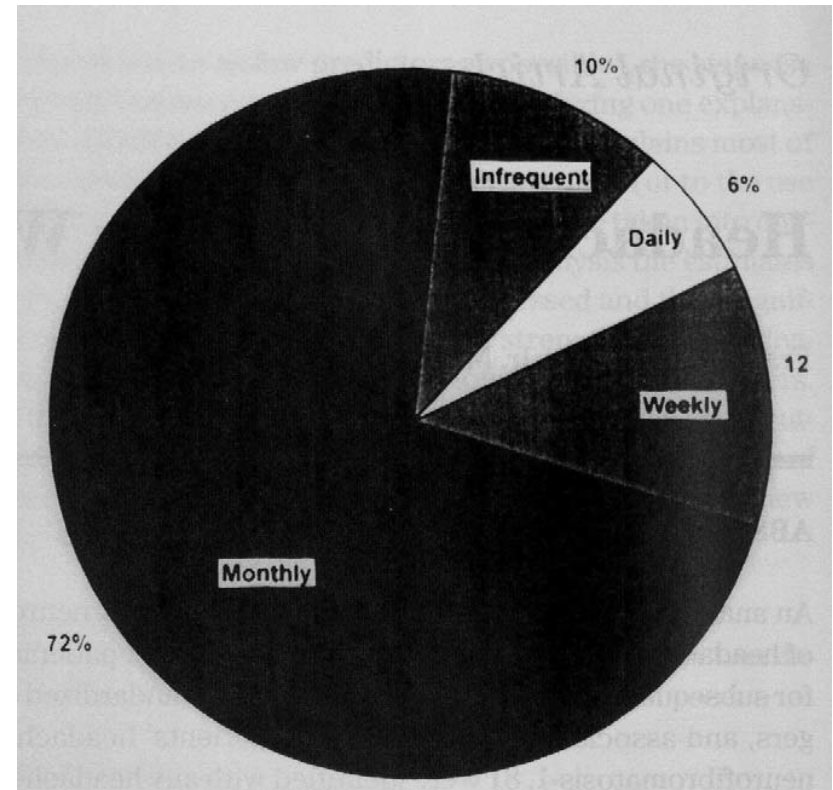
- Self report questionnaire of 181 patients with NF1
  - Avg age 22 (Range 3-85 years)
- Headache present in 30%
  - 7-14 years: 54%
  - 15-18 years: 33%
  - >18: 28%
- Primary headache in 52/55 patients with headache
  - 10% migraine
  - 90% TTH
- Associated with brain tumor in 3
- No correlation with “severity” of NF1
- Conclusion: HA frequency and severity equivalent to general population and not an indication for neuroimaging



# Characterizing Headaches in NF1

DiMario FJ Jr, Langshur S. Headaches in patients with neurofibromatosis-1. *J Child Neurol.* 2000;15(4):235-238.

- 81 patients with NF1
  - Mean age 20.9 years (range: 5-49 years old, only 7 patients >18 years old)
- Any Headache: 61%
- Recurrent Headache: 47%
- 88% had onset <20 years old
- Classification
  - 34% migraine
  - 45% with tension type headaches
  - 15% mixed headache type
  - 7.5% with "other" head pain
- Common triggers identified
  - Stress (32%)
  - Changes in weather (13%)
  - Menstruation or fatigue (12%)
  - Specific foods (6%)
  - Post-ictal (4%)
  - Reading (3%)
- 2/81 (2.5%) had tumor related headaches
  - 100% had abnormal neurologic exams



# How Does This Compare To The General Population?

- Sao Paulo, Brazil
  - 100 subjects (50% with NF1, 50% without)
  - Mean age: 13.2 years old (range: 4-19)
- Headache ( $p < 0.001$ )
  - NF1: 62%
  - Control: 14%
- Migraine ( $p < 0.001$ )
  - NF1: 54%
  - Control: 14%
- Mean age of onset of HA in NF1: 8 years old
- Mean HA Frequency in NF1 patients: 11.3 days/month
- Imaging: 2/50 patients with NF1 had tumors causing headaches
  - Pediatr Int. 2014 Dec;56(6):865-867.
- US study of >8500 NF1 pts
  - higher odds of health insurance claims for epilepsy (OR = 7.3), migraine (OR = 2.6), headache (OR = 2.9), MS (OR = 1.9), PD (OR = 3.1), sleep disturbances (OR = 1.4)
  - <18 years old: Headache (OR = 3.4), Migraine (OR = 3.9)
  - Headache association the same even if accounting for brain tumors
    - Genet Med. 2015 Jan;17(1):36-42.



# Should We Always Get an MRI?

- Routine labs, LP, EEG and neuroimaging are not needed in patients with a normal exam and no “red flags”
- American Academy of Neurology Practice Parameter:
  1. Obtaining a neuroimaging study on a routine basis is not indicated in children who have recurrent headaches and normal results on neurologic examination.
  2. Neuroimaging should be considered in children who have abnormal results on neurologic examination, the coexistence of seizures, or both.
  3. Neuroimaging should be considered in children in whom there are historical features to suggest the recent onset of severe headache, change in the type of headache, or if there are associated features that suggest neurologic dysfunction.

## Headache red flags

Less than 6-month duration

Confusion

Abnormal neurologic exam

Lack of visual aura

Vomiting

Sleep-related headaches

Lack of family history of migraine

Progressive course

Acute, severe onset

Change in headache description or diagnosis

Consistently worse in the morning

Worsening with Valsalva

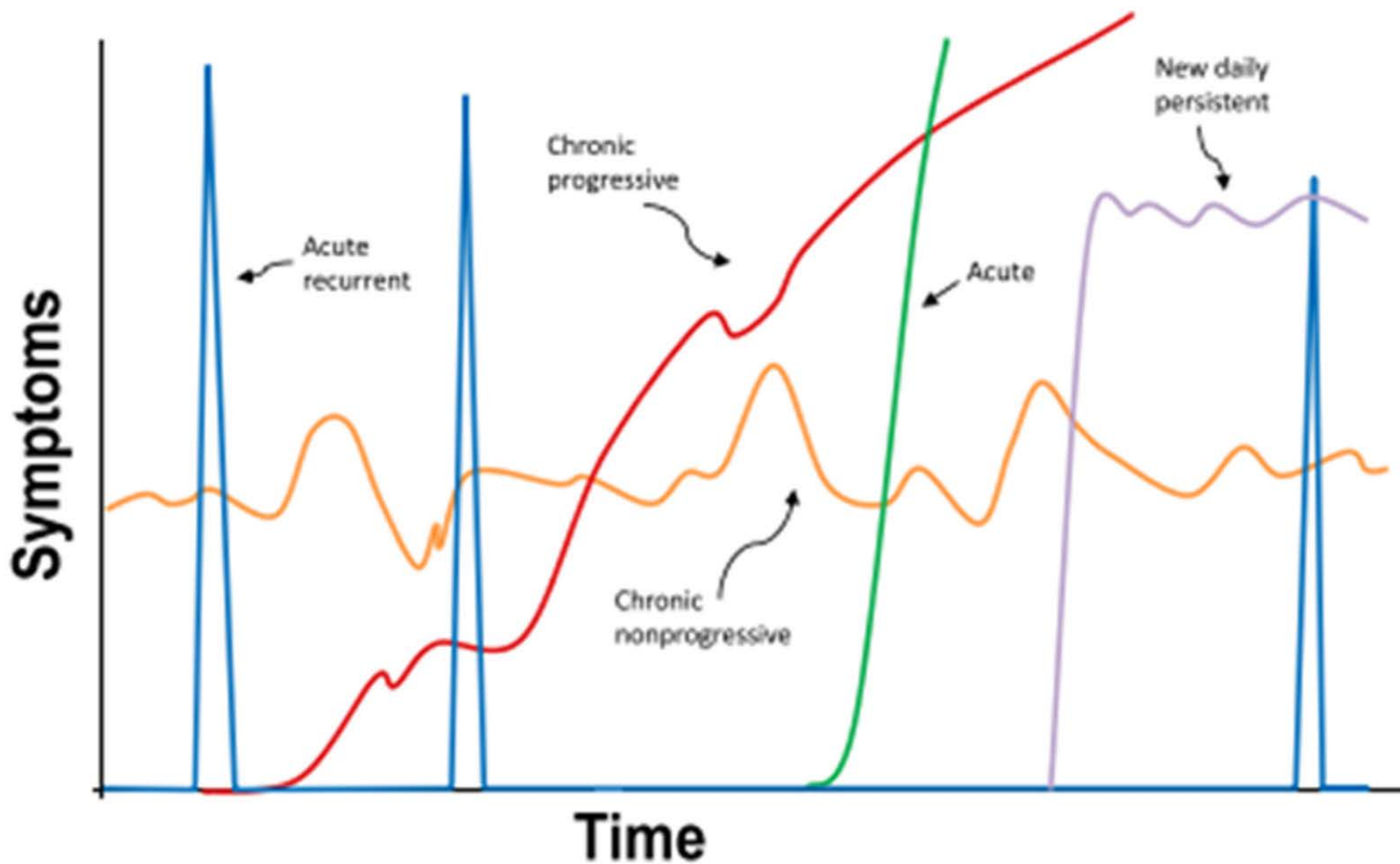
Positional headaches

Comorbid seizures

Symptoms of systemic illness



Curr Probl Pediatr Adolesc Health Care. 2017 Mar;47(3):44-65.



# Do Headaches Affect Quality of Life in NF1?

Afridi SK, Leschziner GD, Ferner RE. Prevalence and clinical presentation of headache in a National Neurofibromatosis 1 Service and impact on quality of life. *Am J Med Genet A*. 2015;167A(10):2282-2285.

- 115 individuals completed a questionnaire
  - Mean age: 36 years (Range: 16-67)
- 78% had headaches
- Migraine: 83% of headache patients, 65% of total
  - Mean onset: 15 years
  - Mean frequency: 6/month
  - Mean HIT-6: 56 (substantial impact)
  - Triggers: sleep disturbance, stress, menstruation
- Tension Type Headache: 11% of headache patients
- Chronic Daily Headache: 11%
  - Chronic Tension Type Headache: 1/10
  - Chronic Migraine: 9/10
    - Mean HIT-6 score: 58 (substantial impact)
    - Only 2/9 on a preventative med
- Majority of patients did not mention headaches until asked about them specifically
- Clearly impactful given HIT-6 scores

TABLE I. Headache Phenotype in 90 NF1 Patients

Headache phenotype	N
Tension-type headache	10
Primary stabbing headache	2
Temporomandibular joint dysfunction	1
Migraine (with/without aura)	75 (15/60)
Probable migraine	2





# Headache Toolbox

## Pediatric Migraine Action Plan (PedMAP)

### Pediatric Migraine Action Plan (PedMAP)

Date: \_\_\_\_\_

Name \_\_\_\_\_ Date of Birth \_\_\_\_\_

Treating Provider: \_\_\_\_\_ Phone: \_\_\_\_\_

Emergency Contact: \_\_\_\_\_ Phone: \_\_\_\_\_

### Headache Information

My diagnosis is: \_\_\_\_\_ Describe aura (if any): \_\_\_\_\_





- Riboflavin (Vitamin B2) 200 mg daily x4 months
- CoQ10 100 mg twice a day x4 months
- Amitriptyline
- Topamax
- Depakote
- Gabapentin
- Beta Blockers
- cGRP inhibitors (>18years old)
- eNeura/TMS
- Nerve Blocks
- Botox

### Green Zone – Prevent more headaches

Do or take this every day to help prevent YOUR headaches:



- Get enough sleep; keep a regular schedule
- Eat healthy foods; don't skip meals
- Drink enough water; avoid caffeine
- Get regular exercise; manage your weight
- Learn ways to relax; manage your stress

*Directions to provider:* Set 1-2 healthy lifestyle goals. Consider a daily medicine or vitamin/ supplement if > 1 headache per week. Consider Cognitive Behavior Therapy (CBT) if PedMIDAS > 10. To download PedMIDAS, visit <https://www.cincinnatichildrens.org/service/h/headache-center/pedmidas>

It may take 4-6 weeks to see a big change, so stick with it! Visit [www.headachereliefguide.com](http://www.headachereliefguide.com) to manage your headaches

### Yellow Zone – Don't wait. Act fast to treat your headaches

Go to school nurse or health office right away. Take your **quick-relief** medicine as soon as your headache starts:

Take \_\_\_\_\_ Dose \_\_\_\_\_

Route \_\_\_\_\_ May repeat after \_\_\_\_ hours.

Take \_\_\_\_\_ Dose \_\_\_\_\_

Route \_\_\_\_\_ May repeat after \_\_\_\_ hours.

Let your provider know if you need to take your quick relief medicines 3 or more days a week or if this plan isn't working.



- Drink some water or sports drink if you can
- Rest in a dark, quiet place for 30 minutes and practice your relaxation exercises (e.g., deep breathing, guided imagery), if you can
- You may need a different PE activity, dark glasses, or a quiet place to work for a while

*Directions to provider:* Goal is pain-free within 1-2 hours for intermittent headaches and back to baseline for constant headaches. Consider NSAID +/- antiemetic, a triptan or a combination of medications.

*Directions to provider:* Optional section for other scenarios, step 2 or a "backup" plan. Home "backup" plan: Consider dopamine blocker +/- diphenhydramine +/- NSAID.

### Red Zone – Time to get more help

Contact your **provider's office** if:

- Your headache is much worse, lasting much longer than usual
- Go to the **Emergency Room** if:
- You have new and very different symptoms like loss of vision, unable to move one side of your face or body, trouble walking or talking, very confused or unable to respond



- Call 9-1-1 if child loses consciousness or has stroke-like symptoms

*Directions to provider:* Avoid giving aspirin to children < 16 years old. Avoid giving opioids or butalbital for pain.

I authorize the quick-relief medication(s) listed in the Yellow Zone:

Provider's Signature \_\_\_\_\_ Date \_\_\_\_\_

Parent/Guardian's Signature \_\_\_\_\_ Date \_\_\_\_\_

- to be administered by school personnel
- to be self-administered by student
- to be administered only by parent

- Fluids – Sports Drink
- Acetaminophen/NSAIDs – Max 3 days/week
- "-triptans" – max 2 days/week
- Prochlorperazine
- No opioids

- IV infusion
- DHE

# Nutraceuticals in NF1

Carotenuto M, Esposito M. Nutraceuticals safety and efficacy in migraine without aura in a population of children affected by neurofibromatosis type I. *Neurol Sci.* 2013;34(11):1905-1909.

- Assessed safety and efficacy of GingkogolideB/Coenzyme Q10/B2/Mg twice a day x6 months
- 18 school age patients
- Migraine frequency pre-treatment: 10.42 attacks/month
- Migraine frequency post-treatment 4.01 attacks
- Intensity decreased from 7.83 → 5.04
- PedMIDAS score decreased from 28.4 → 6.0



# The Cycle of Pain and Stress

Kongkriangkai AM, King C, Martin LJ, et al. Substantial pain burden in frequency, intensity, interference and chronicity among children and adults with neurofibromatosis Type 1. *Am J Med Genet A*. 2019;179(4):602-607.

- Ages 8-17 and 18-40
- Survey data
- 49 participants (28 children)
  - Median age of children: 12 years old
- 55% report regularly experiencing pain (46% of children)
- 41% (29% of children), reported pain on 3 or more days/week
- 41% overall reported relatively high HA frequency (32% of children)
  - Most had migraine phenotype (38% in children)
- Patients with pain more likely to report diagnosis of anxiety and/or depression

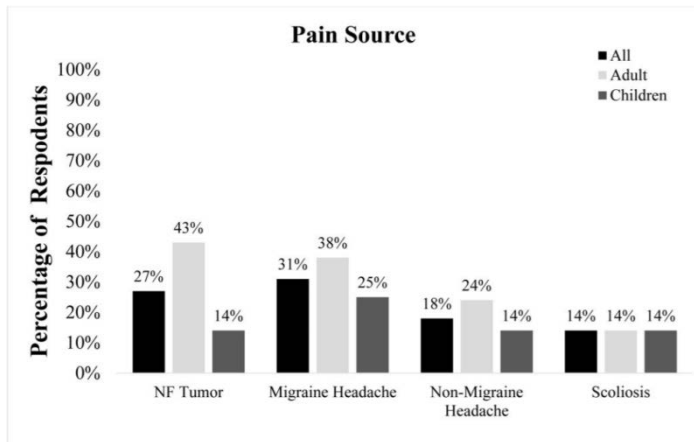


Figure 3.  
Reported source of pain in children and adults with NFI (N=49)

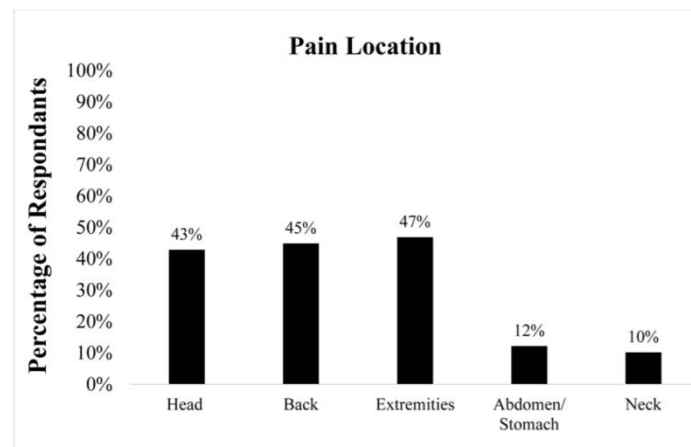


Figure 1.  
Location of pain reported in children and adults with NFI (N=49)



# Pediatric Migraine Action Plan (PedMAP): Headache Toolbox

Tools for life	
Children and adolescents with headaches need to learn how to manage life with headaches at home, at school and with friends.	
<b>Cognitive Behavior Therapy (CBT)</b>	CBT teaches you new ways of thinking about pain and new ways of responding to it by setting goals, pacing activity, and using your brain to turn down your body's pain response. Visit <a href="http://www.findcbt.org/FAT/">http://www.findcbt.org/FAT/</a> to learn more about CBT and find a therapist.
<b>Biofeedback</b>	A machine uses sensors to measure your stress level and a computer screen shows you how your stress level changes as you practice different stress-reducing exercises. Visit <a href="https://www.bcia.org">https://www.bcia.org</a> to learn more about biofeedback and find a therapist.
Tools for home	
Your brain works best when it knows what to expect. Keeping your brain in balance can prevent more migraines. Visit <a href="https://www.healthychildren.org">https://www.healthychildren.org</a> for advice on healthy living and <a href="http://www.headachereliefguide.com">www.headachereliefguide.com</a> to make a plan.	
<b>Hydration</b>	Drink enough water to make your urine pale. Drink more water when it's hot outside and before, during and after you exercise. Avoid drinks with caffeine and added sugar.
<b>Food</b>	Don't skip meals. Choose fresh fruits, vegetables, whole grains, and lean protein when you can. Avoid foods high in salt, sugar or corn syrup, or with many chemicals listed on the label.
<b>Sleep</b>	Teens need 8-10 hours and pre-teens need 9-12 hours of sleep each night. Keep a regular schedule. No electronics 30 minutes before bedtime. Report snoring or breathing difficulty.
<b>Exercise</b>	Try to exercise every day. To lose weight, you need 20-30 minutes of activity strong enough to make you sweat. Be sure to warm up first and don't exercise past the point of pain.
<b>Emotions</b>	Stress is part of life and learning to deal with it is important for growth. Learn and practice positive coping strategies. Avoid over-scheduling and allow some downtime to de-stress.
Tools for school	
Students with headaches can struggle to focus and may take longer to finish their schoolwork. This added stress can lead to more headaches and even more frequent absences. Ask school officials to create an <b>Individualized Health Plan</b> or <b>504 Plan</b> using some of these strategies to combat the specific migraine symptoms that are preventing a student from functioning properly at school.	
<b>Trigger Management:</b>	<ul style="list-style-type: none"> <li>• Allow student to keep a water bottle at his/her desk</li> <li>• Allow student to use restroom when needed</li> <li>• May need to eat a mid-morning and/or mid-afternoon snack</li> <li>• May need access to a quiet place to eat lunch with a companion</li> <li>• May need an anti-glare screen filter or paper copies of assignments</li> <li>• May need to use a rolling backpack or obtain a second/digital copy of books for home</li> <li>• Other: _____</li> </ul>
<b>Symptom Management:</b>	<ul style="list-style-type: none"> <li>• Allow student to go to nurse/health office as soon as his/her headache or aura starts</li> <li>• Allow student to rest for 30 minutes before returning to class</li> <li>• Allow light-sensitive student to wear dark glasses for a few hours when pain is severe</li> <li>• Allow noise-sensitive student to work in a quiet place (i.e., library) for a few hours when pain is severe</li> <li>• Allow a PE alternative (e.g., walking, stretching, yoga) when pain is severe</li> <li>• Other: _____</li> </ul>
<b>Workload Management:</b>	<ul style="list-style-type: none"> <li>• May need extended time to take tests or complete work when headache is severe</li> <li>• May need a copy of class notes/homework packet when absent or unable to concentrate</li> <li>• May need extra time to make up exams or assignments missed due to severe headache</li> <li>• Consult school psychologist to evaluate for suspected learning problems</li> <li>• Consider modifying assignments (fewer problems, test of mastery) or class schedule (half days, rest breaks, fewer classes) if returning to school after an extended absence</li> <li>• Other: _____</li> </ul>



# Children's National Headache Program





# Children's Urgent Headache Program

202-476-HEAD or [headache@childrensnational.org](mailto:headache@childrensnational.org)



Children's National.





## CHILDREN'S NATIONAL HEADACHE PROGRAM



Although headaches are common in children, recurrent or frequent headaches that interfere with daily life are a concern. The Headache Program is a specialized clinic within the Division of Neurology that evaluates and treats more than 2,000 patients annually.

The clinic helps children and adolescents with chronic, debilitating head pain, headaches and migraines. We work to identify the cause and find an effective way to help children manage their headaches.

### Features of our program include:

-  Headache infusions – patients with acute exacerbation of headache disorders can be given intravenous infusions in an outpatient setting to alleviate their pain rapidly and get them back to school and activities
-  Interdisciplinary headache evaluations – patients with chronic debilitating headaches have the option of seeing an interdisciplinary team of experts including neurologists, behavioral pain medicine specialists, anesthesiologists, and neurosurgeons, who aim to provide a comprehensive approach to pain management
-  Urgent headache appointments – most patients can be scheduled within five business days of calling to see a headache expert and provide urgent management
-  Integrative, multi-disciplinary team including:
  - Neurologists
  - Anesthesiologists
  - Pain psychologists
  - Physical therapists
  - Advance practice providers including NPs and PAs
  - Physical Medicine
  - Nursing

## Don't let frequent headaches interfere with your child's daily life.

Children's National Interdisciplinary Intractable Headache Clinic utilizes lifestyle modification and healthy habits, alternative medicine, pain-focused cognitive behavioral therapy, biofeedback, nerve blocks and infusions to provide additional treatment options for kids.

Our team works together to identify the cause of headaches in children and find effective ways to help manage them. For urgent appointments, call: 202-476-HEAD (4323)

Pediatric Specialists  
of Virginia



[www.childrensnational.org/departments/headache-program](http://www.childrensnational.org/departments/headache-program)



Children's National™

# Urgent Headache Team

Children's National Health System



- 5 Attending Physicians
- 1 Nurse Practitioner
- 50-100 Urgent Access Appointments Weekly
  - Annapolis, DC, Fairfax, Frederick, Friendship Heights, Laurel, and Rockville
- **TELEMEDICINE AVAILABLE!!!**

# Comprehensive Headache Team

Children's National Health System



- Behavioral Pain Medicine – 1 PsyD, 1 Intern, 1 Extern, 1 Fellow
- Anesthesia/Pain Medicine - Nerve Blocks, Trigger Point Injections, Botox, Acupuncture
- Physical Therapy – 2 PTs doing desensitization, range of motion, pain de-amplification
- Neurosurgery - Occipital nerve stimulator, Neuro-interventional Procedures
- Clinical Coordinator – Urgent Appointments, Chronic Headache Multidisciplinary Appointments
- Headache Nurse – Urgent Headache Needs, Forms, Authorization
- Headache Infusion Center – 2 beds x 5 days per week, two nurses, coordinator
- Research Assistant – Multiple internal protocols and Clinical Trials



# Children's National Headache Research Program

- Since 2017 research program development:
  - Over 75 lectures regionally and nationally
  - 10 publications including CHAMP in NEJM
  - 16 abstracts
  - 10 IRB protocols
    - **Medication Overuse Headache** – natural history longitudinal study; enrolling patients 1-17yo with suspected MOH
    - **Screen Use and Headache** – survey on association between handheld screen use and headache; closed
    - **Joint Hypermobility and Headache** – study on association between joint hypermobility and pain disability; data analysis
    - **Headache Registry** – natural database on all patient characteristics; enrolling
    - **New Daily Persistent Headache** – retrospective analysis of population frequency and clinical characteristics; data analysis
    - A Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Crossover Study to Evaluate the Efficacy and Safety of **Zolmitriptan Nasal Spray** for the Treatment of Acute Migraine in Subjects Ages 6 to 11 Years, With an Open-Label Extension; enrolling
    - Clinical and Translational Science Institute at Children's National **App Hackathon**: Using Artificial Intelligence for Headache Research and Management in development
    - A Phase 3, Randomized, Double-blind, Placebo controlled, Parallel Group Study to Evaluate the Efficacy and Safety of **Erenumab in Children (6 to < 12 Years) and Adolescents (12 to < 18 Years) With Episodic Migraine**; enrolling
    - A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of **Erenumab in Children (6 to < 12 Years) and Adolescents (12 to < 18 Years) With Chronic Migraine** ; enrolling
    - **Functional and psychosocial correlates** of youth with chronic pain disorders (10-18 Years); enrolling

# Conclusions

- Headache is a common problem
- It may be even more prevalent in patients with NF1
- The presence of headache does not always require an MRI in patients with NF1
- Healthy habits are the foundation of treatment, including hydration, exercise, sleep, and diet goals
- Instruct patients on the interaction of pain and stress and provide resources to reduce stress
- Children's National's Headache Program for education and urgent headache management



# Acknowledgments


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- William Gaillard – Chief Neurology
- Roger Packer – VP Neurosciences

### Urgent, Specialized Headache Care for Kids: TRUST THE EXPERTS

Although headaches are common in children, recurrent or frequent headaches that interfere with daily life are a concern to both parents and children.


At Children's National Health System, we care for more than 2,000 patients annually using a comprehensive and holistic approach to management, including lifestyle modification, behavioral strategies and advanced medications to alleviate your child's pain.



 For urgent appointments, call 202-476-HEAD (4323) from 8:30 a.m. to 4:00 p.m. Monday through Friday to speak with a trusted headache expert.

The Headache Team offers the following services to their patients and families:

- Urgent headache appointments – scheduled within five business days
- Interdisciplinary headache evaluations – patients with chronic debilitating headaches have the option of seeing an interdisciplinary team of experts
- Headache infusions

  
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