

# THE NEW ERA OF MIGRAINE: HOPE AND HELP

*ANDREW CHARLES MD*



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# EXCITING TIMES FOR MIGRAINE – PROGRESS & HOPE



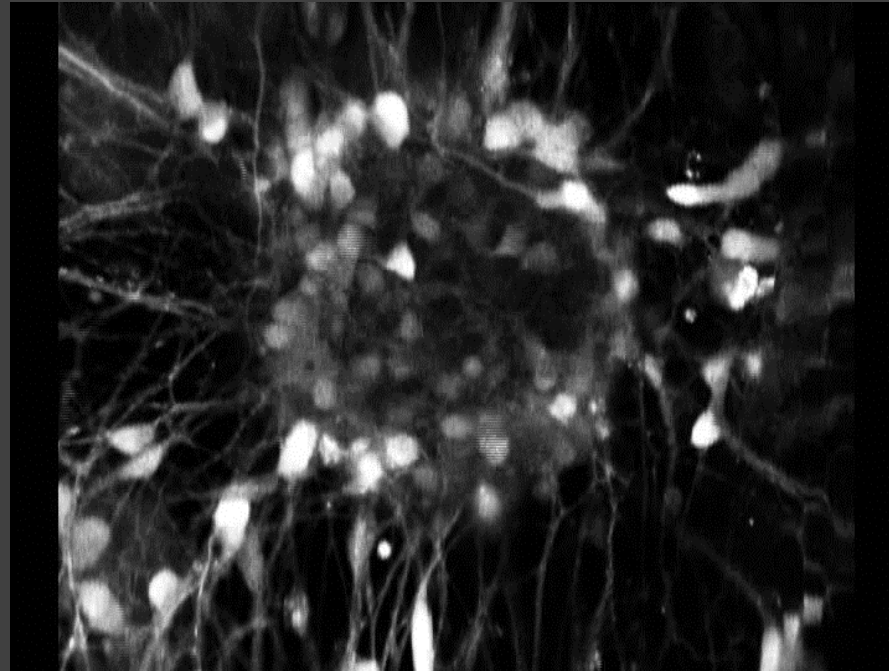
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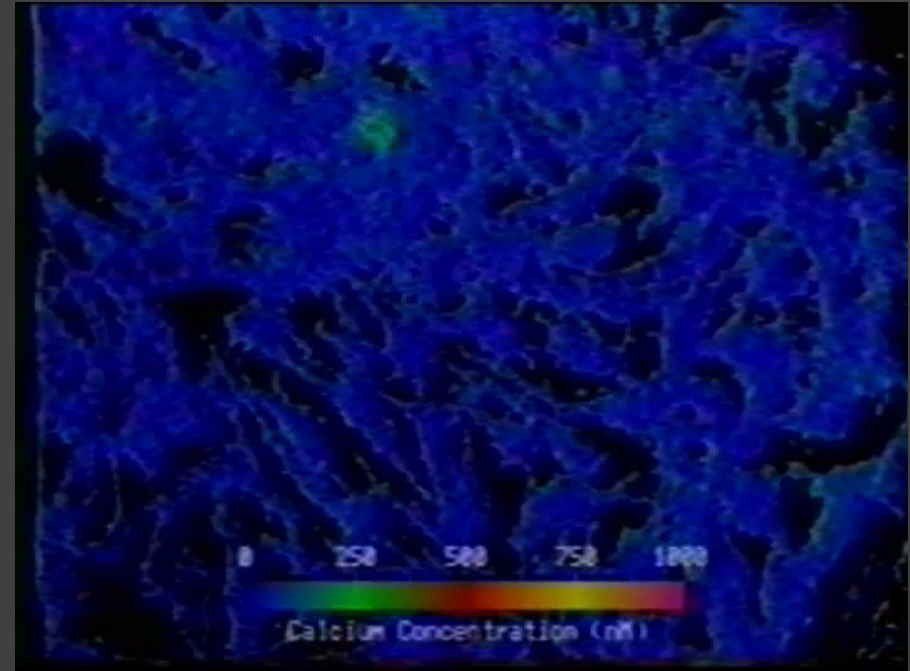
# A JOURNEY IN HEADACHE MEDICINE...



**Cool Scientist**



**Brain Cell Communication**



**Glial Cells in Action**

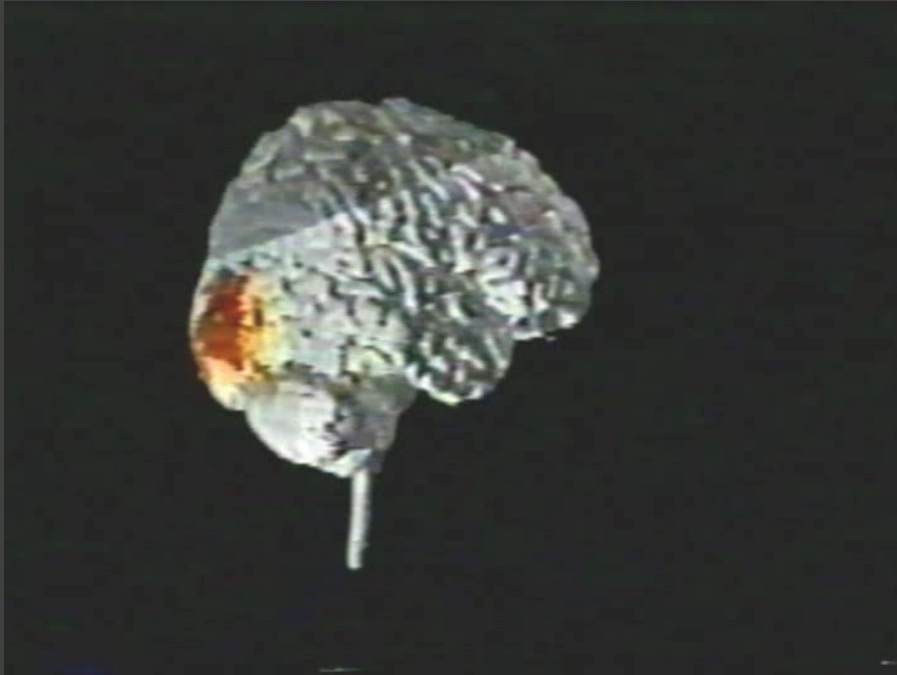


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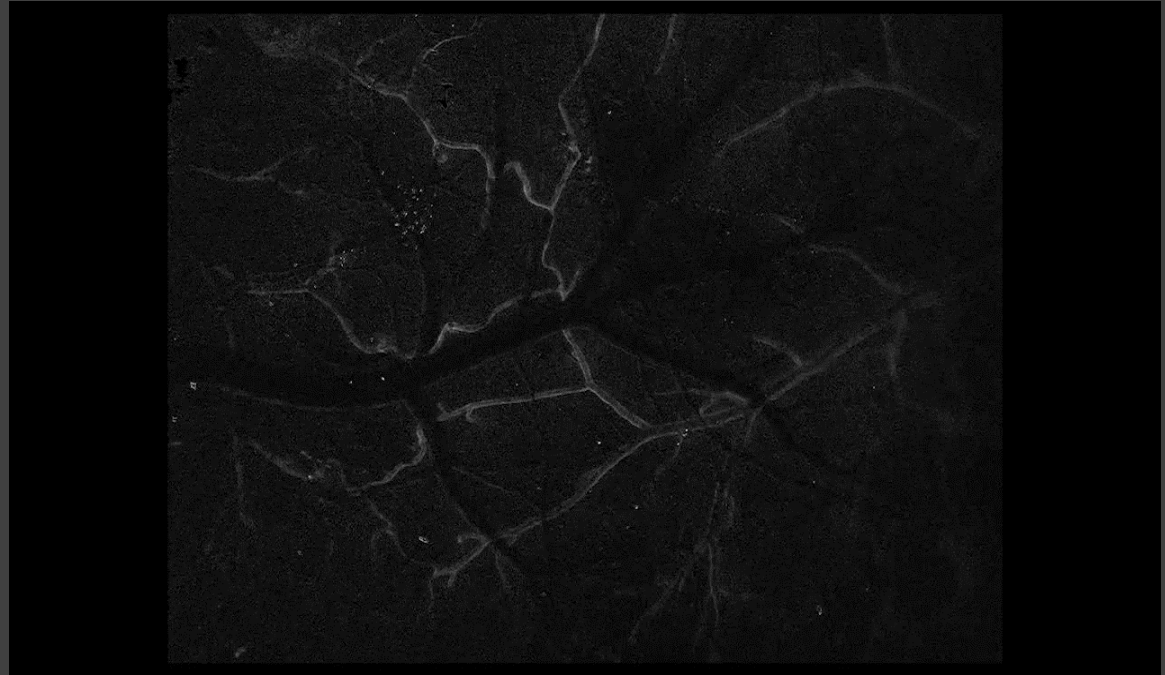
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# CORTICAL SPREADING DEPRESSION & MIGRAINE



**PET Scan showing waves of brain activity during a migraine attack**



Andrew C. Charles and Serapio M. Baca

**nature**  
REVIEWS **NEUROLOGY**



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# MIGRAINE IS AN EXTRAORDINARILY INTERESTING AND IMPORTANT PROBLEM IN NEUROSCIENCE



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# MIGRAINE IS THE SECOND LEADING CAUSE OF TIME SPENT DISABLED OF ALL DISORDERS ON THE PLANET

## Most Disabling Disorders (YLDs) 2016



1	Low Back Pain
2	Migraine
3	Age-related Hearing Loss
4	Iron-deficiency Anaemia
5	Major Depression
6	Neck Pain
7	Other Musculoskeletal Disorders
8	Diabetes
9	Anxiety Disorders
10	Falls
11	COPD
12	Osteoarthritis
13	Acne Vulgaris
14	Refraction And Accommodation
15	Schizophrenia

16	Asthma
17	Ischaemic Stroke
18	Dermatitis
19	Opioid Use Disorders
20	Other Mental And Substance
21	Dysthymia
22	Alcohol Use Disorders
23	Bipolar Disorder
24	Edentulism
25	Neonatal Preterm Birth
26	Epilepsy
27	Diarrhoeal Diseases
28	Tension Headache
29	Ischaemic Heart Disease
30	Other Sense Organ Diseases



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# DO THE MATH



**Maya**

Migraine begins at **age 12**,  
ends at **age 65** (approx. 53 yrs.)

**2 days**  
per month

Grand Total =  
1,272 days with migraine

**3.5 years of life**  
in migraine prison

**8 days**  
per month

Grand Total =  
5,088 days with migraine

**14 years of life**  
in migraine prison

**20 days**  
per month

Grand Total =  
12,720 days with migraine

**35 years of life**  
in migraine prison



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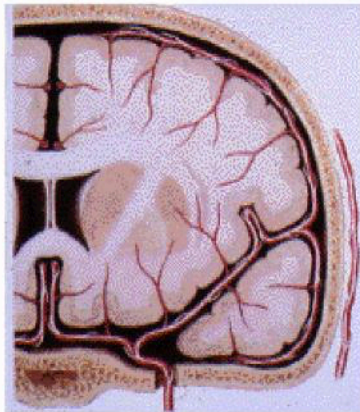
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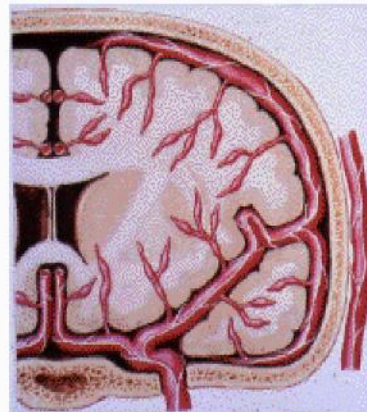
# SHIFTING PARADIGMS OF MIGRAINE

## Vascular Theory of Migraine

**Aura Phase**  
Spasm



**Headache Phase**  
Vasodilation



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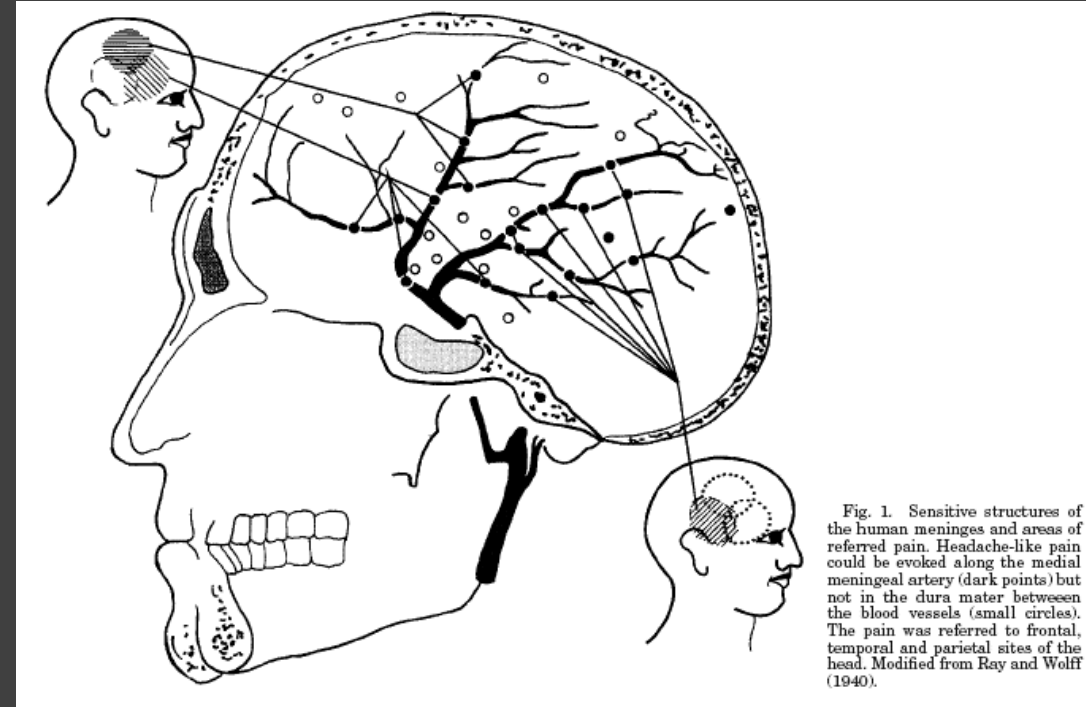


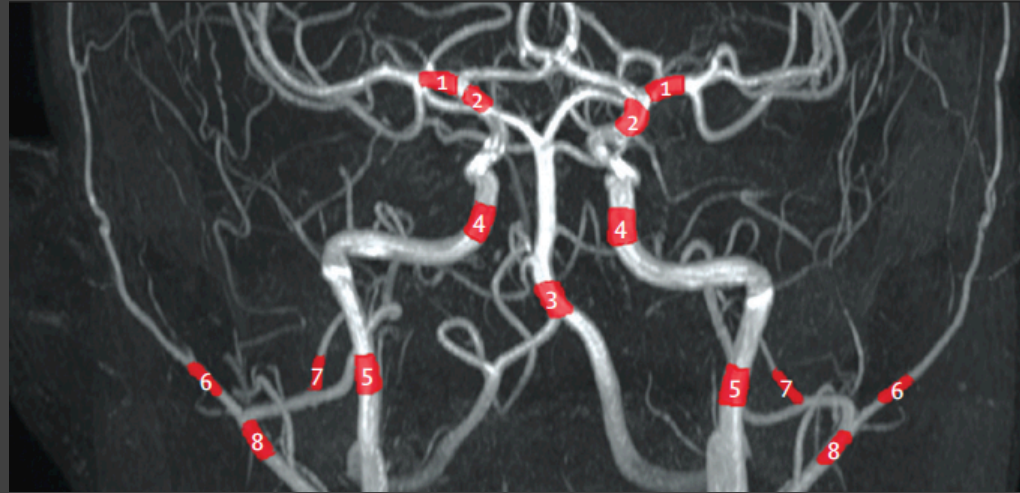
Fig. 1. Sensitive structures of the human meninges and areas of referred pain. Headache-like pain could be evoked along the medial meningeal artery (dark points) but not in the dura mater between the blood vessels (small circles). The pain was referred to frontal, temporal and parietal sites of the head. Modified from Ray and Wolff (1940).



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# BLOOD VESSELS DO NOT CAUSE MIGRAINE PAIN



**Magnetic resonance angiography of intracranial and extracranial arteries in patients with spontaneous migraine without aura: a cross-sectional study**

*Faisal Mohammad Amin, Mohammad Sohail Asghar, Anders Hougaard, Adam Espe Hansen, Vibeke Andrée Larsen, Patrick J H de Koning, Henrik B W Larsson, Jes Olesen, Messoud Ashina*



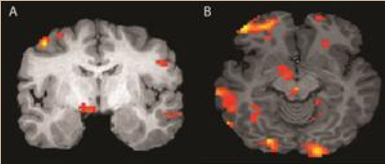


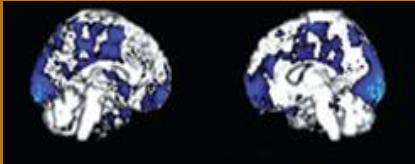
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# TIMELINE OF A MIGRAINE

EVOLUTION OVER 4 – 72 HOURS

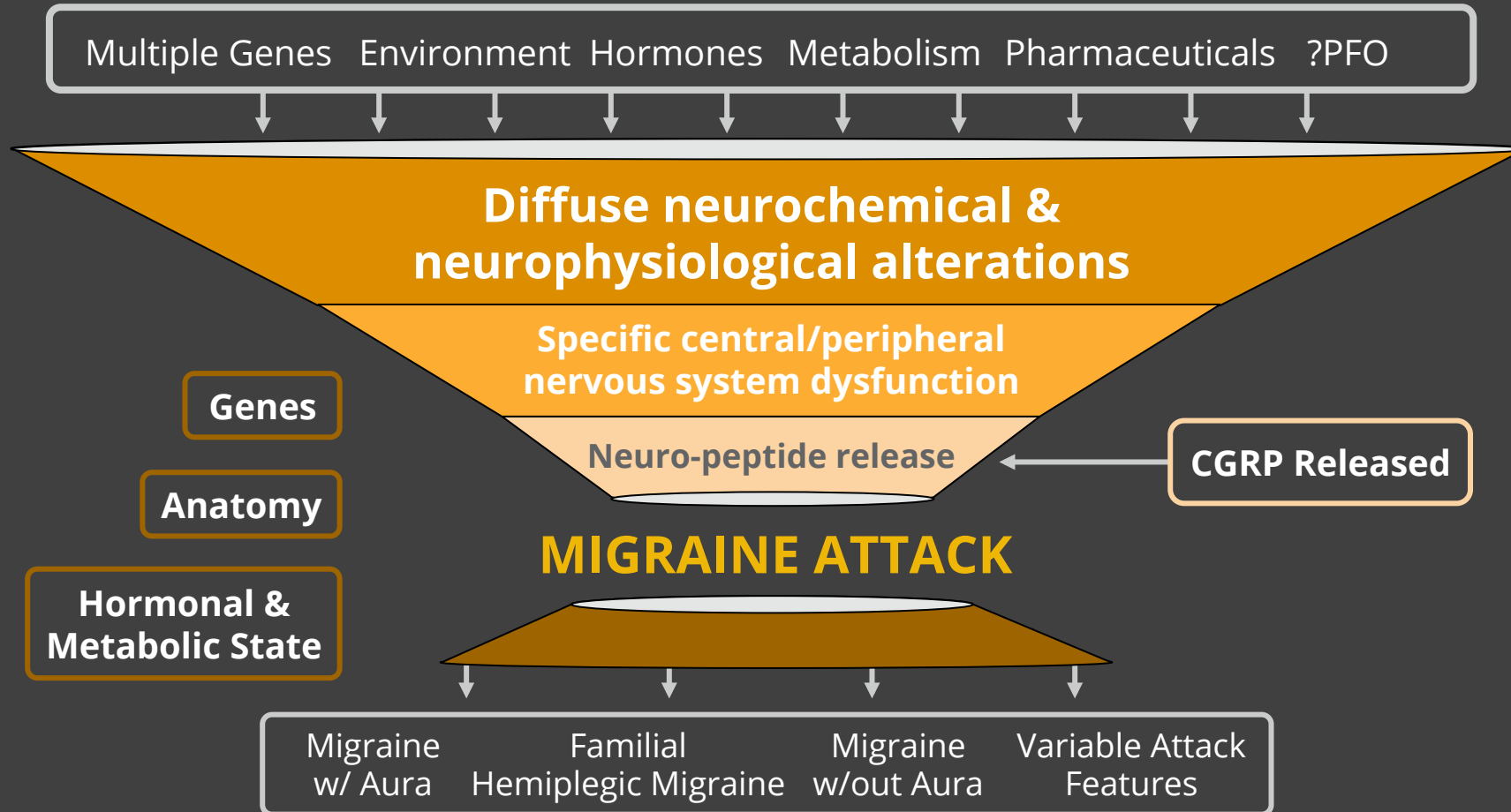
PREMONITORY	AURA	HEADACHE	POSTDROME
Yawning   Frequent urination			
Neck Pain   Fatigue   Mood change	Light sensitivity   Sound sensitivity		
	Nausea   Vomiting		
	Visual symptoms   Sensory symptoms   Language symptoms   Cognitive symptoms		
		Headache	
		Touch-sensitivity	
Hypothalamus Brainstem Cortex	Cortex	Brainstem Thalamus Hypothalamus	Cortex Thalamus Hypothalamus
			



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# THE PATHOPHYSIOLOGY OF MIGRAINE: IMPLICATIONS FOR CLINICAL MANAGEMENT



THE LANCET  
Neurology



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# THE CGRP STORY

CGRP Administration  
Triggers Migraine

CGRP Levels are Elevated  
in Chronic Migraine

CGRP is Released  
During a Migraine Attack

Small Molecule CGRP  
Antagonists Abort Migraine

FDA Approval of anti-CGRP  
monoclonal antibody therapies  
for migraine prevention

1990

*Goadsby et al.*

2002

*Lassen et al.*

2004

*Olesen et al.*

2013

*Cernuda-Morollon et al.*

2018



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# INJECTABLE MONOCLONAL ANTIBODIES TARGETING CGRP

	<b>Erenumab</b> <b>Aimovig</b>	<b>Galcanezumab</b> <b>Emgality</b>	<b>Fremanezumab</b> <b>Ajovy</b>	<b>Eptinezumab</b>
<b>Studied for</b>	Episodic Migraine, Chronic Migraine	Episodic Migraine, Chronic Migraine, Episodic Cluster Headache, Chronic Cluster Headache	Episodic Migraine, Chronic Migraine, Episodic Cluster Headache, Chronic Cluster Headache	Episodic Migraine, Chronic Migraine
<b>Dosing</b>	Monthly SC Autoinjector	Monthly SC Autoinjector	Monthly or Q3 month SC Syringe; IV load for Chronic Migraine	Q3 month IV
<b>Target</b>	<b>CGRP receptor</b>	<b>CGRP peptide</b>	<b>CGRP peptide</b>	<b>CGRP peptide</b>
<b>Regulatory status as of March, 2019</b>	<b>FDA Approved May 17, 2018</b>	<b>FDA Approved September 14, 2018</b>	<b>FDA Approved September 27, 2018</b>	Presented (+) Phase 3 Episodic Migraine; Continuing Phase 3 Chronic Migraine



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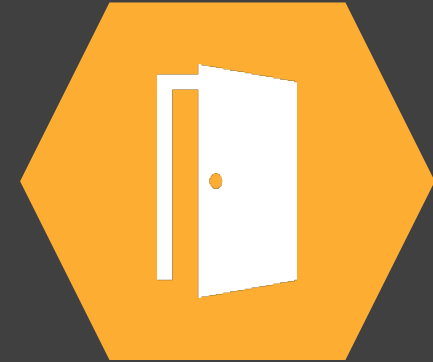
# WHY THE CGRP STORY IS SUCH GOOD NEWS



It Validates  
Migraine Biology



Demonstrates  
Migraine-specific  
Treatments



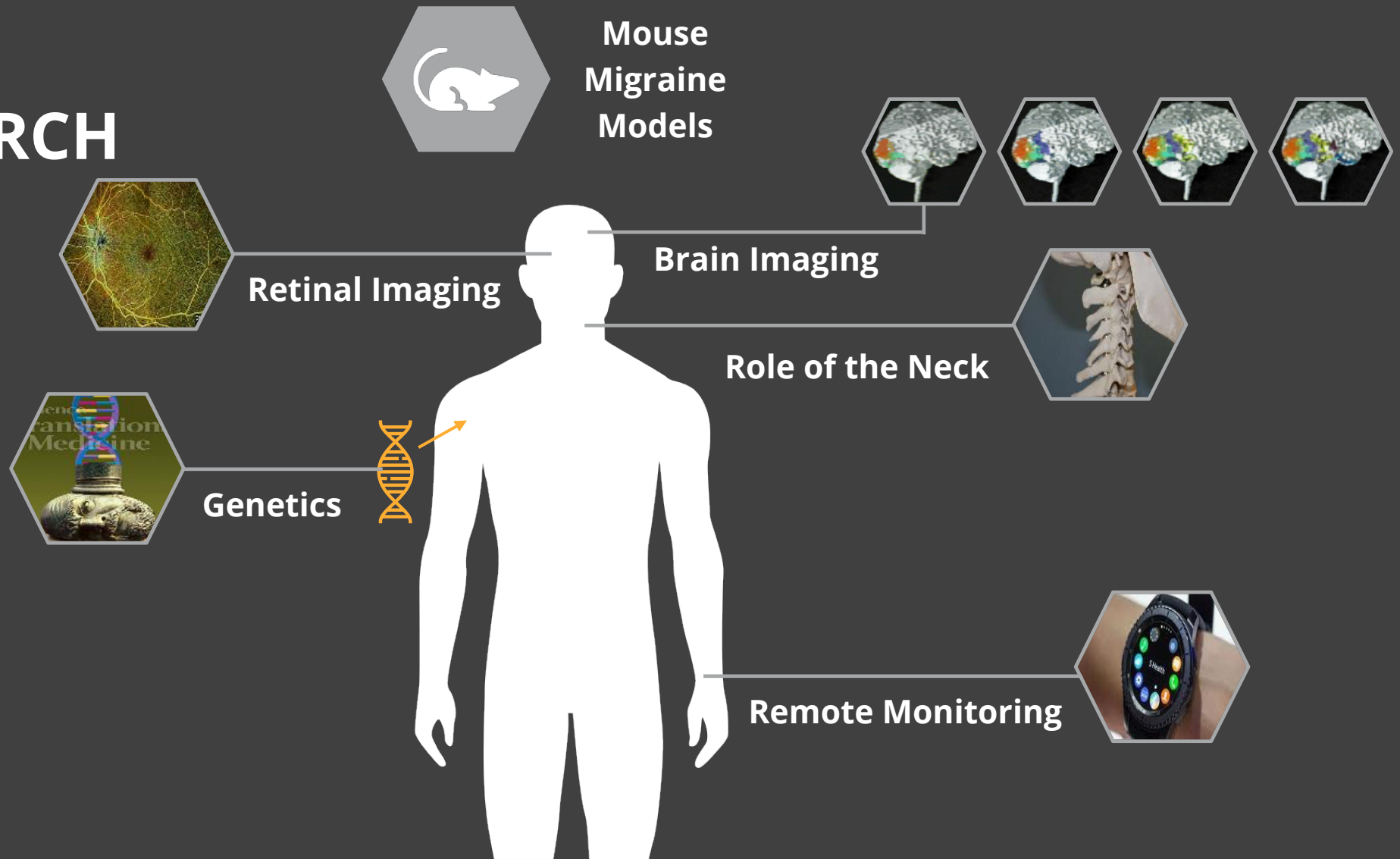
Opens The Door To  
Precision Medicine



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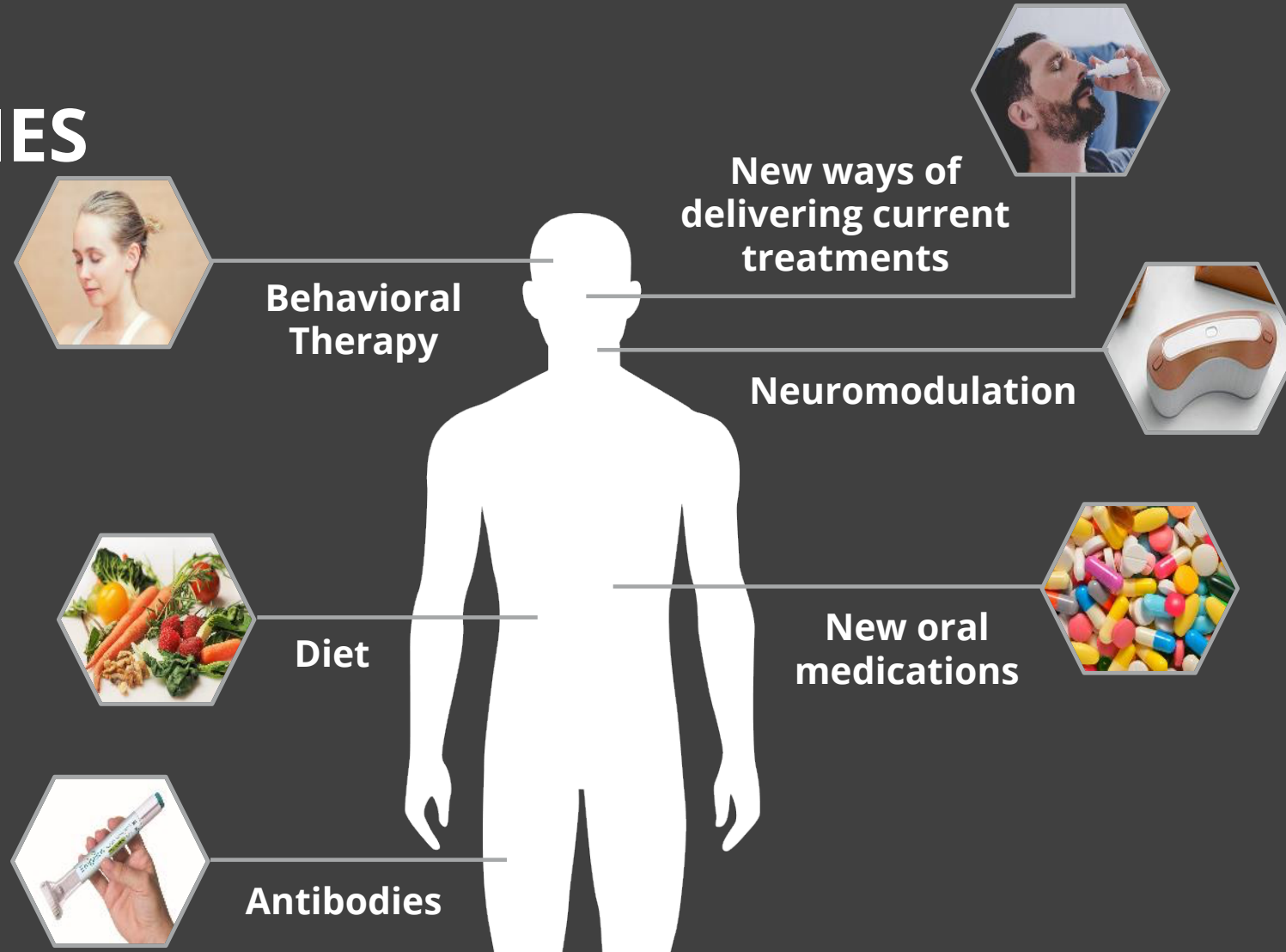
# RESEARCH



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# THERAPIES



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