


Movement Disorders & Artificial Intelligence

From Clinical Signs to Digital Biomarkers

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What Are Movement Disorders?

Movement disorders (MDs) are neurological conditions where the main clinical problem is an **abnormality of movement** — the nervous system fails to control the body or body parts normally.

Too Little Movement

Bradykinesia — slowness and reduction of voluntary movement

Too Much Movement

Tremor, dystonia, chorea, tics, dyskinesia

Why AI? Movement is not just clinically observable — it can be **measured, recorded, quantified, and analyzed**, making MDs a compelling domain for AI-driven diagnostics and monitoring.

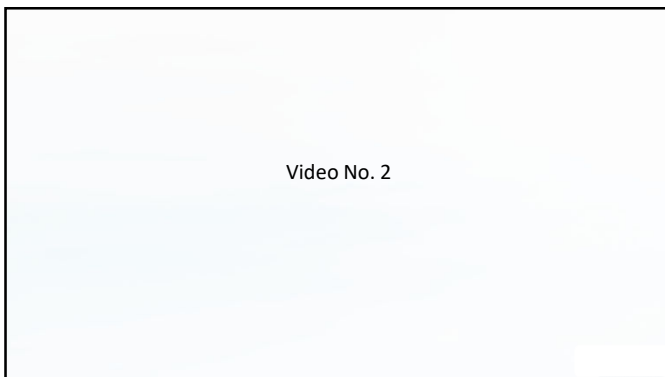


Why Are Movement Disorders Attractive for AI?

The main clinical sign is often **visible**.
A neurologist examines how the patient moves — how fast, how regular, whether movement is symmetric, and whether it changes during action, rest, walking, speaking, or emotional stress.
These features can be translated into **measurable variables**.

<p>Neurologist Observes</p> <ul style="list-style-type: none"> • Speed of movement • Regularity • Symmetry • Changes during action, rest, walking, or emotional stress 	<p>AI Measures</p> <ul style="list-style-type: none"> • Speed & frequency • Acceleration • Rhythm • Variability
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*The neurologist gives **MEANING**, an AI gives **MEASUREMENT** to a movement.*



Parkinson's Disease as a Central Model

- Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease, traditionally recognized by its motor symptoms.
- It primarily affects movement but also many non-motor functions.
- It develops due to the gradual degeneration of dopaminergic neurons in the brain, leading to a dopamine deficit that disrupts motor control and beyond.

<p>Core Motor Signs</p> <ul style="list-style-type: none"> • Bradykinesia — Slowness of movement; essential for diagnosis • Rest tremor — Typically a "pill-rolling" tremor, most prominent at rest • Rigidity — Increased muscle tone causing stiffness and resistance to passive movement • Postural instability — Impaired balance and coordination, often a later feature 	<p>Non-Motor Symptoms</p> <ul style="list-style-type: none"> • Cognitive impairment — Ranging from mild deficits to dementia • Depression & anxiety — Among the most common psychiatric manifestations • Sleep disorders — Including REM sleep behavior disorder and insomnia • Autonomic dysfunction — Orthostatic hypotension, constipation, urinary issues • Hypoemia — Reduced sense of smell; often an early marker • Fatigue — Persistent tiredness unrelated to exertion
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Why is Parkinson disease the central model?

The key clinical feature is **bradykinesia** — slowness of movement. Other important motor signs include **rigidity**, **rest tremor**, **postural instability**, gait impairment, and fluctuation of motor symptoms.

PD is one of the most common neurodegenerative disorders, and its importance is increasing worldwide

2x

Prevalence Doubled

According to WHO, the prevalence of PD has doubled over the last 25 years.

11.8M

Current Global Prevalence

25M

Projected by 2050

Projections indicate that the number of people living with PD could reach 25 million by 2050, mainly because of population aging and growth.

PD is a central model for the use of AI because it is common, progressive, clinically measurable, and requires monitoring over time.

Bradykinesia: The Core Motor Sign of PD

Clinical Observation

Bradykinesia (BK) is the central motor sign of PD — in simple words, the patient moves slowly.

Bradykinesia is examined by asking the patient to perform *rapid repetitive movements*, such as:

- finger tapping
- hand opening and closing
- pronation-supination movements

AI-Measurable Features

- Movement speed
- Amplitude
- Rhythm & regularity
- Pauses or hesitations
- Left-right asymmetry

Key message: BK is not just slow movement; it is a measurable pattern of reduced speed, amplitude, rhythm, and automaticity. It can be measured using video analysis, sensors, or signal processing.

Video No. 3

Tremor: Rhythmic Movement as a Measurable Sign

Tremor is an involuntary, rhythmic, oscillatory movement of a body part. Clinically, we describe not only whether tremor is present or not — we also describe where it appears, how fast it is, how large the movement is, whether it is regular, and under which condition it occurs (rest, posture, or action).

Frequency

Parkinsonian tremor ~4–6 Hz

Amplitude

How large the movement is

Rhythm

Whether it is regular or not

Body distribution

It may affect one hand, both hands, the legs, the head, the jaw, the voice...

Conditions

Under which conditions it occurs (rest, posture, action)

Rigidity

Rigidity means increased resistance to passive movement.

In PD, it has specific characteristics:

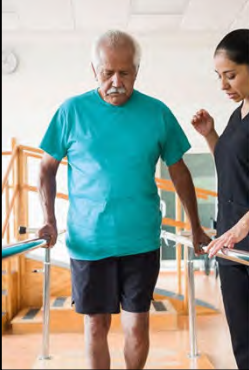
- constant through the range of motion
- not dependent on movement speed
- often asymmetric
- may have a cogwheel quality



Rigidity is more challenging for AI than other core motor signs, because it is not directly visible on video.

Key message: Rigidity reminds us that not every neurological sign is equally easy to digitize.





Gait and Postural Instability in PD

Parkinsonian gait - slow, with short steps and reduced arm swing.

Later in the disease, patients may develop:

- hesitation during gait initiation
- shuffling gait
- festination (progressively faster and shorter steps that may appear uncontrolled)
- freezing of gait

Related to independence, safety and quality of life

From the perspective of AI and digital biomarkers, gait is especially interesting because many features can be objectively analyzed and quantified.

We can analyze:

- gait speed
- step length
- gait variability
- asymmetry
- turning
- balance and postural stability
- freezing episodes

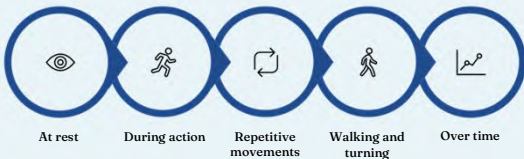
Key point: Gait is not only a clinical observation — it is a complex motor pattern that can be digitally measured and analyzed over time.




How Neurologists Examine Movement

Neurological examination is **structured observation** - changing conditions, observing responses, and interpreting patterns. This logic is very close to signal analysis.

Observing movement



AI can transform structured observation into structured measurement.



What AI Can Do in Parkinson's Disease

- Quantify Movement**
Extract speed, amplitude, frequency, rhythm, asymmetry from video or sensor data
- Detect Patterns**
Identify tremor, bradykinesia, dyskinesias, and on/off periods
- Analyze Speech**
Process language as a digital signal for additional biomarkers
- Monitor Over Time**
One clinical visit is a snapshot - digital tools create a continuous picture

What AI Cannot Do in Parkinson's Disease

AI Cannot Replace

- **Clinical reasoning and full clinical context**
AI can detect patterns, but it cannot understand the whole patient. AI does not know the full history, medication state, comorbidities, examination findings, and patient priorities.
- **Safe decision-making from poor-quality data**
If the video, sensor signal, or input data are poor, AI output may be unreliable.
- **Independent treatment decisions**
AI can support assessment, but treatment decisions must remain clinical decisions.
- **The patient-neurologist relationship**
Empathy, trust, explanation, and shared decision-making cannot be replaced by AI.

Key message: AI can support clinical assessment, but it cannot replace clinical judgment.


Example: AI analysis of speech in Parkinson's disease

RESEARCH ARTICLE

Cognitive Phenotyping of Parkinson's Disease Patients Via Digital Analysis of Spoken Word Properties

Francis J. Ferrante, MS^{1,2}, Denise Escobar-Groves, MS^{1,2}, Maria Fernanda Lopez, BS^{1,2}, Ramona Lopez de Carlos, PhD^{1,2}, Lucas Pedraza-Soriano, BS¹, Jai M. J. Vitor, PhD¹, Pedro Chandi Quevedo, MD^{1,3}, Claudio Estévez, PhD^{1,2}, Eugenia Hesse, PhD^{1,2}, Lucia Amoruso, PhD^{1,2}, Juan Rafael Orozco Arroyave, PhD^{1,2}, and Adolfo M. Garcia, PhD^{1,2,4*}

- A good example of AI application beyond motor symptoms
- Language output was transformed into measurable digital features related to cognition
- Machine learning models were used to predict cognitive status and to classify patients with Parkinson's disease with and without mild cognitive impairment
- Their results showed that digital word-property analysis could predict cognitive symptom severity and help distinguish patients with and without mild cognitive impairment.



AI Video Analysis in Parkinson's Disease: A Systematic Review of the Most Accurate Computer Vision Tools for Diagnosis, Symptom Monitoring, and Therapy Management
Lazzaro di Biase^{1,2}, Pasquale Maria Piccirilli^{1,2} and Francesco Bogamelli^{1,2}

- *Systematic Review (45 studies investigating AI assessment in PD)*
- Gait, bradykinesia, tremor, facial expression, posture and balance can all be quantified using ordinary video recordings
- Gait was the most frequently analyzed motor symptom
- Results frequently correlate with expert findings
- Need for guidelines for video-recording protocols and software usage are for widespread clinical implementation

Take home messages

- AI can **objectively quantify motor signs** in Parkinson's disease
- Video, sensors, and speech analysis capture features **difficult to assess** by routine clinical observation
- AI can support **diagnosis, monitoring, and therapy assessment**
- AI **cannot replace** clinical reasoning and the patient-physician relationship
- Further **validation, standardization, and ethical implementation** are necessary

Stroke




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Q/A

- What is a Stroke?
- Signs and symptoms of a stroke
- Stroke risk factors and prevention
- Stroke treatment and care
- What to remember?

What is a Stroke?

- Stroke is a disease that affects the arteries of the brain.
- A stroke occurs when a blood vessel bringing blood to the brain gets blocked (ischemic) or ruptures (haemorrhagic).
- The affected part of the brain doesn't get the oxygen and nutrients it needs, causing brain cells to die.
- A stroke is a medical emergency. Immediate treatment may minimize the long-term effects of a stroke and even prevent death.



Stroke Facts

- Stroke is a "brain attack."
- Although stroke is more common after age 55, it can also happen at any age and at any time.
- Leading cause of adult disability:
 - Some people who have a stroke will make a full recovery.
 - But more than 2/3 of survivors will have some type of disability.
- Every 40 seconds, someone in the U.S. has a stroke.
- Two million brain cells die every minute during a stroke.

How Common is Stroke?

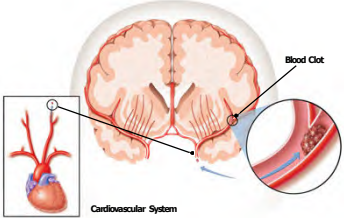
- Stroke has a large impact on society, with **more than 9 million** stroke survivors in the U.S.
- Every year, about **800,000 people** in the U.S. have a stroke, with about 185,000 being recurrent strokes.
- Stroke is the **5th leading** cause of death in the U.S. (**3rd leading cause of death in women**)
- About **55,000 more** women than men have a stroke each year.
- Black people are **twice as likely** as white people to have a first-time stroke.
- Treatment may **reduce the effects of stroke** if administered soon after the onset of symptoms.

Up to 80% of strokes may be prevented with lifestyle changes.

Ischemic stroke

Ischemic stroke is the most common type of stroke, accounting more than 75% of strokes.

An ischemic stroke occurs when a clot blocks a vessel supplying blood to the brain. The artery becomes narrowed or clogged, cutting off blood flow to brain cells.



Transient Ischemic Attack

TIA, is a temporary blockage of blood flow to the brain. The clot usually dissolves on its own or gets dislodged. TIAs produce symptoms just like a stroke, but typically last a shorter amount of time.

While a TIA doesn't cause permanent damage, it's a "warning stroke" signaling a possible full-blown stroke ahead.

A TIA's temporary symptoms make diagnosis challenging.

Here is what you can expect:

- Assessment for symptoms and medical history
- Imaging of the blood vessels in the head and neck
- Other testing such as head CT, angiography and MRI

Once TIA is diagnosed, a follow-up visit with a neurologist is recommended to assess your risk of future stroke.

Hemorrhagic Stroke

A hemorrhagic stroke happens when a blood vessel bursts (ruptures) in the brain. This type of stroke may affect large arteries in the brain or the small blood vessels deep within the brain. The rupture keeps the surrounding areas of the brain from getting oxygen.

Hemorrhagic strokes are less common than ischemic strokes, accounting for about 13% of strokes. However, they are associated with a higher risk of death.

Use the letters in F.A.S.T. to spot a stroke:

<p>F = FACE</p> <p>Does one side of the face droop or is it numb?</p> <p>Ask the person to smile. Is the person's smile uneven?</p>	<p>A = ARMS</p> <p>Is one arm weak or numb?</p> <p>Ask the person to raise both arms. Does one arm drift downward?</p>	<p>S = SPEECH</p> <p>Ask the person to repeat a simple phrase. Is their speech slurred or strange?</p>	<p>T = TIME</p> <p>If you observe any of these signs, act quickly</p> <p><i>Note the time when any of the symptoms first appear.</i></p>
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Other Symptoms of Stroke

Watch for Sudden:

<p>NUMBNESS or weakness of the face, arm or leg, especially on one side of the body</p>	<p>CONFUSION, trouble speaking or understanding speech</p>	<p>TROUBLE SEEING in one or both eyes</p>	<p>TROUBLE WALKING, dizziness, loss of balance or coordination</p>	<p>SEVERE HEADACHE with no known cause</p>
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Act Quickly

If you experience one or more of these symptoms or notice them in someone else, even for a short time.

- Medical options may reduce the effects of stroke
- Time is of great importance, as treatment must be administered soon after the onset of symptoms
- Stroke strikes quickly. You should too!
- Why you must learn to recognize stroke symptoms — F.A.S.T.
 - To save lives
 - Easy to remember
 - Easy to teach
 - Requires quick action

The effects of stroke depend on various factors:

<p>Region of the brain that is affected</p>	<p>Size of the area that is damaged by the stroke</p>	<p>Functions that the damaged area controls</p>
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Stroke Recognition: 5 Steps to Stroke Recognition

How a Stroke Can Affect You

A stroke on the **left side of the brain** affects the right side of the body and you may experience some difficulties with:

- Weakness and loss of sensation on the right side of the body
- Speech and language difficulties (aphasia)
- Inability to read, write and learn new information
- Slow, cautious behavioral style
- Reduced ability to do math, reason and analyze things
- Memory loss

How a Stroke Can Affect You

A stroke on the **right side of the brain** affects the left side of the body and you may experience some difficulties with:

- Weakness and loss of sensation on the left side of the body
- Depth perception or directions
- Vision problems
- Quick, inquisitive behavioral style
- Inability to paint or appreciate art and music
- Lack of ability to recognize emotions in someone's voice
- Memory loss

Risk Factors that cannot be controlled:

- Age:** While strokes can occur at any age, risk increases after age 55.
- Gender:** Women have a lower risk than men before menopause, but more women than men die of stroke.
- Family history:** Strokes appear to have a genetic link. You face a higher risk if an immediate family member has had a stroke.
- Race and Ethnicity:** Black people have a higher prevalence of stroke and a higher death rate from stroke than any other racial group.
- Prior stroke or transient ischemic attack (TIA):**
 - A person who's had TIA has a one in three more likelihood of having a stroke than someone of the same age and sex who hasn't.
 - If you had a stroke, it means you are at a greater risk for another stroke. Almost 1 in 4 will experience a recurrent stroke in the next 5 years.

Medical Risk Factors

- High Blood Pressure:** Measurement of 120/80 mm Hg and above is considered high blood pressure. You need to work with your health care professional to manage your blood pressure. Talk to your doctor as your number may be different for someone over 65.
- Cholesterol:** Buildup of fatty deposits and other cells in artery walls.
- Circulation Problems:** Strokes can be caused by blockage in your arteries and veins that carry blood through your heart to your brain.
- Diabetes:** Having diabetes more than doubles your risk of stroke. High blood glucose increases plaque buildup and damage in your arteries.
- Atrial Fibrillation (AFib):** AFib increases stroke risk fivefold.

Lifestyle Risk Factors

- Quit Tobacco Use and Vaping:** Current smokers have a 2 to 4 times increased risk of stroke compared with nonsmokers or those who have quit smoking more than 10 years ago.
- Eliminate or Reduce Alcohol Use:** Heavy drinking can increase your risk for stroke. Recommendation is no more than two drinks per day for men and no more than one drink per day for non-pregnant women. Pregnant people should not drink alcohol.
- Maintain a Healthy Weight:** Obesity and excessive weight can put a strain on the entire circulatory system.
- Increased Physical Activity:** Physical activity can help reduce stroke risk. A brisk 30 minute walk each day can improve daily health (that's just 15 minutes each way!). Aim for at least 150 minutes of moderate to vigorous-intensity physical activity per week.
- Eat a Healthy Diet:**
 - Rich in fresh fruit, vegetables and whole grains
 - Include a variety of proteins (lean meats, fish, beans, tofu)
 - Minimally processed foods
 - Limit salt intake
 - Limit intake of added sugars
 - Avoid fried foods

In case of a stroke, diagnosis will help determine the type of stroke and its treatment. In the emergency room, the stroke team may:

Ask you when the symptoms of the stroke started. This is critical in determining the best treatment.

- Ask you about your medical history.
- Do a physical and neurological examination.
- Have certain lab (blood) tests done.
- Do a **CT (computed tomography) or MRI (magnetic resonance imaging) brain scan. This determines what kind of stroke a person has had.**
- Study the results of other diagnostic tests that might be done.

Stroke scales

1. Prehospital & Emergency Recognition (Out-of-Hospital)

- ✓ **Cincinnati Prehospital Stroke Scale (CPSS):** A highly sensitive screening tool that tests three physical indicators
- ✓ **Los Angeles Prehospital Stroke Screen (LAPSS):** Uses patient history and physical exams

2. Acute Severity & Neurological Function (In-Hospital)

- ✓ **NIH Stroke Scale (NIHSS):** The gold standard in clinical settings. This 15-item evaluation measures overall neurological function—including level of consciousness, vision, motor strength, sensory, and language. Higher scores indicate greater impairment.
- ✓ **Glasgow Coma Scale (GCS):** While not exclusively a stroke scale, it is crucial for assessing comatose patients or those suffering from hemorrhagic strokes by scoring eye-opening, verbal response, and motor response.

3. Functional Outcome & Recovery (Post-Stroke)

- ✓ **Modified Rankin Scale (mRS):** The most common tool for measuring global disability.
- ✓ **Barthel Index:** Evaluates basic personal care and mobility activities

Prevention

1. Eat Better
2. Be More Active
3. Quit Tobacco
4. Get Healthy Sleep
5. Manage Weight
6. Control Cholesterol
7. Manage Blood Sugar
8. Manage Blood Pressure

STROKE TREATMENT AND CARE

STROKE UNITS

- o Stroke Units are a specialist hospital wards where stroke patients are cared for by a team of professionals who specialise in stroke care
- o Stroke patients are more likely to be alive and living independently a year after having a stroke when cared for on a dedicated stroke unit than patients cared for on regular wards

Hyper-acute Stroke Units (HASU)

- o HASUs bring experts and specialist equipment for the emergency treatment of stroke under one roof to provide world-class treatment, 24 hours a day, seven days a week

STROKE TREATMENT AND CARE

THROMBOLYSIS or MECHANICAL THROMBECTOMY

Thrombolytic therapy is the administration of drugs called lytics or “clot busters” to dissolve blood clots that have blocked major blood vessels. Mechanical thrombectomy is the removal of a blood clot using mechanical devices, and it is performed by an interventional radiologist.

- o Treatment must begin within a certain time of symptom onset. This can restore blood flow to the part of the brain blocked
- o Main complication is bleeding
- o Every patient is assessed as being eligible, but not everyone receives thrombolysis for a variety of reasons. It is the decision of the stroke consultant

WHAT TO REMEMBER - SIGNS AND SYMPTOMS

A SUDDEN ONSET of the following may indicate stroke*

	SYMPTOMS A LOVED ONE MAY EXPERIENCE	SIGNS YOU MAY NOTICE
B Balance	Loss Of Balance: Unstable with less coordination, stumbling, unable to walk straight	Wobbling around, grabbing onto a stationary object, tripping over nothing
E Eyes	Dizziness: Feeling faint, lightheaded, or like the room is spinning	Uncoordinated movements (like motion sickness), like they are drunk (without having any alcohol)
F Face	Vision Changes: Blurred vision or trouble with eyesight in one or both eyes	Squinting or rubbing their eyes, not able to read
A Arms	Facial Drooping: One side of the face is drooping or looks uneven	Ask the person to smile and observe their face. See if the face droops on one side
S Speech	Severe Headache: Pain or discomfort in the head, scalp, or neck with no known cause	Touching their head, rubbing their temples, sensitivity to light
T Time	Weakness: Lack of strength in the arm or leg—especially on one side of the body	Wanting to sit or lay down, difficulty doing simple tasks
	Numbness: A tingling feeling in the body (ie, face, arm, or leg), like pins and needles	Constant touching, massaging, or shaking of the numb areas
	Trouble Speaking: Unable to speak or slurred speech	Sentences that can't be understood, difficulty having a conversation
	Confusion: Unable to understand what is happening, can't think clearly or feel thrown off	A puzzled look, raised or wrinkled eyebrows, shaking their head "no"; "a hard time focusing, trouble making decisions

Time To Call 911

*Note that these symptoms or a combination of them are not unique to stroke, but if they are sudden and out of the ordinary, they may indicate a sign of stroke and require immediate attention.

Cerebrovascular diseases are an area where time, localization, and workflow are crucial.

Clinical evaluation includes:

- time of onset of symptoms or last-known-well time,
- symptoms and signs,
- ischemic vs. hemorrhagic stroke,
- CT/CTA/CTP or MRI,
- assessment for thrombolysis or thrombectomy,
- prevention,
- rehabilitation.

Medical specialization included: transport, emergency department, neurologist, radiologist, laboratorist, interventional radiologist and physical medicine and rehabilitation

Cooperation

Potential AI projects:

- automatic detection of bleeding on CT,
- detection of early ischemic changes,
- detection of large vessel occlusion,
- analysis of perfusion maps,
- prediction of outcome after thrombolysis/thrombectomy,
- prediction of hemorrhagic transformation,
- prehospital triage,
- analysis of speech and facial asymmetry,
- digital recovery monitoring,
- robotics and AI in rehabilitation,

Possible LLM applications:

- last-known-well time extraction from notes or calls
- identification of missing data in the stroke pathway,
- summarizing contraindications from medical history
- structuring the imaging report,
- generation of handover between emergency, neurology and stroke unit,
- discharge summary after stroke,
- educating the patient about prevention
- rehabilitation and follow-up plan.

ELITE OF
NEURO
LOGY



CLINIC OF
NEUROLOGY

HEADACHE MIGRAINE Y OR N?

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WHAT WE ARE GOING TO TALK ABOUT TODAY

- Headaches – are they normal?
 What exactly is a migraine?
- Diagnosing the headache type
- Medical management
- Potential cooperation

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IS IT NORMAL TO HAVE A HEADACHE?


- No, but people think so because it is so overwhelming common
- Most people with HA don't go to the doctor
- Affects 37 million people (estimated)
- Most headaches are migraines, but...







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EVERY HEADACHE IS NOT A MIGRAINE

Headache
Migraine



Headaches can be a symptom of illness Migraines ARE the illness

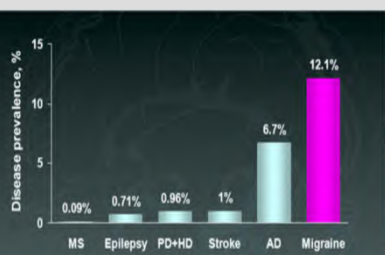
Sinus	Cluster	Tension	Migraine
 Sinus pain is behind browbone and/or cheekbones.	 Cluster pain is in and around one eye.	 Tension pain is like a band squeezing the head.	 Migraine pain, nausea and visual changes are typical of classic form.

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PRIMARY HEADACHES


Feature	Tension Headache	Migraine	Cluster Headache
Sensation	Dull, aching pressure	Throbbing, pulsing pain	Sharp, stabbing, burning
Location	Both sides ("head band")	One side of the head	Strictly around one eye
Duration	Hours to days	4 to 72 hours	15 to 180 minutes
Activity	Can push through it	Forces you to lie down	Causes restlessness/pacing

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Disease	Prevalence (%)
MS	0.09%
Epilepsy	0.71%
PD+HD	0.96%
Stroke	1%
AD	6.7%
Migraine	12.1%

MS = multiple sclerosis; PD+HD = Parkinson's disease + Huntington's disease; AD = Alzheimer's disease. Adapted from Hertz D et al. Neurology. 2007;68:328-337.



1

MIGRAINE IS A DISORDER OF BRAIN EXCITABILITY AND SENSORY DYSMODULATION CAUSING HEAD PAIN AND ASSOCIATED FEATURES

Migraine involves activation of the trigeminovascular system, neural input from trigeminal and cervical neurons, projections to vessels, dura mater and venous sinuses, and convergence to trigeminal nucleus caudalis. This can explain the distribution of pain, which often includes anterior and posterior regions of the head and the upper neck.

Stimulation of the trigeminal ganglion results in release of vasoactive neuropeptides, including calcitonin gene-related peptide (CGRP)

Sensitization refers to the process in which neurons become increasingly responsive to nociceptive and non-nociceptive stimulation

IS IT A MIGRAINE?

- Pain in any part of the head and neck can be a migraine, **unilateral** or bilateral
- Quality varies: Pressure, **stab**, throb, hammer, etc.
- **Nausea, vomiting**
- **Photo-, phono-, osmo-phobia.**
- Visual, sensory, and language auras
- Missing work/ life events due to headache

IS IT A MIGRAINE?

- **ID Migraine:**
- 3 simple questions: Have you in the past 3 months
 - Felt nauseated with a headache?
 - Had photophobia with a headache?
 - Been limited in your ability to function because of a headache?

SCIENTIFIC FINDINGS ARE TRANSFORMING THE UNDERSTANDING OF MIGRAINE

Migraine is not "just" a headache¹

2nd leading cause of years lived with disability worldwide²

Molecular targets have been identified for the development of migraine-specific therapies^{3,4}

Effective treatment can reduce migraine frequency and risk of progression to more severe disease^{5,6}

Diagnosis is a critical first step to optimal migraine management^{6,7}

¹ Russo AF. Ann Rev Pharmacol Toxicol. 2010;50:553-562. ² Global Burden of Disease and Injury Incidence and Prevalence Collaborators. Lancet. 2017;390:1211-1259. ³ Borsook D, et al. Neurol Clin Pract. 2015;5:317-325. ⁴ Charlin A, Lambert Neuro. 2016; 17:174-182. ⁵ Lipton RB, et al. Headache. 2007;47:52-55. ⁶ Bigley K, Stewart WF. Headache Clin Neuro. 2015;151:447-462. ⁷ Weatherall MN. The Adv Chronic Dis. 2015;6:115-123.

MIGRAINE ATTACK 4-72H

Migraine is a clinical diagnosis. According to the ICHD-3 classification, headaches are classified based on a combination of duration, pain characteristics, associated symptoms, and recurrence pattern. ICHD-3 is the basic international reference system for headache classification.

MIGRAINE MAY INTENSIFY, LEADING TO INCREASED DISABILITY

No migraine

↔

0-4 headache d/mo

↔

5-9 headache d/mo

↔

10-14 headache d/mo

↔

≥15 headache d/mo

- EM progresses to CM at an average rate of approximately 2-3% per year
- Inadequate management of acute migraine can double the risk of progression
- Risk factors for progression to CM include:
 - Greater headache frequency
 - Medication overuse
 - Use of opioids or barbiturates
 - Certain comorbidities, e.g. anxiety

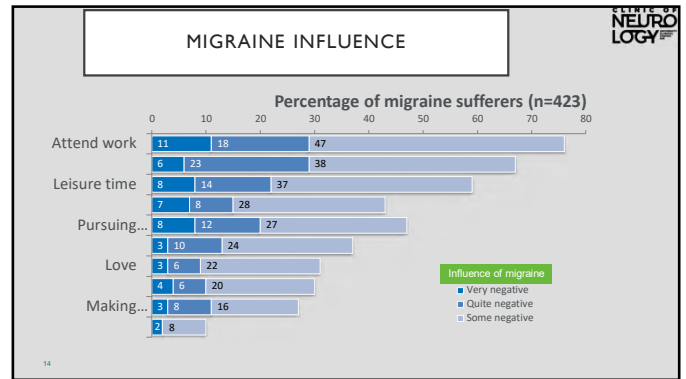
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MIGRAINE IS ASSOCIATED WITH COMORBIDITIES, INCLUDING PSYCHIATRIC DISORDERS

- Anxiety¹⁻³
- Depression¹⁻³
- Hypertension²⁻⁵
- Allergies & sinusitis^{1,2,5}
- Sleep disorders³⁻⁵
- GI disorders^{1,2,3,5}
- Epilepsy^{1,2,4}
- Chronic pain disorders¹⁻⁵

Comorbidities:

- Contribute to the disabling effects of migraine
- Can be bi-directional
- Add challenges to migraine management
- May affect treatment choice and patient adherence



SECONDARY HA?

- **Sudden "Thunderclap"**: Pain that hits maximum intensity within 60 seconds.
- **The "Worst Ever"**: A completely new type of pain you've never felt before.
- **Systemic Signs**: Headache accompanied by fever, a stiff neck, or confusion.
- **Physical Triggers**: Headaches brought on by coughing, sneezing, or sudden exercise.
- **Focal neurological deficits on exam**
- **New HA in the elderly**
 - Think about structural lesion/tumor; No CT/MRI indicated unless red flag symptoms/ findings on exam.

<5 % of headache patients will have a structural lesion

IMPORTANT QUESTIONS

- Is it a primary headache (migraine, for example) or a secondary headache?
- If it is secondary, what is the cause?
- If it is primary, what is the best treatment option?

TABLE 1: SNNOOP10 MNEMONIC

S	Systemic symptoms (ie, fever)
N	Neoplasm in history
N	Neurologic deficit or dysfunction
O	Onset of headache is sudden or abrupt
O	Older age (typically greater than 50)
P10	Pattern change, positional headache, precipitated by valsalva, papilloedema, pregnancy or puerperium, painful eye with autonomic features, post-traumatic onset, pathology of the immune system, medication overuse, or new drug use (pills)

HEADACHE TREATMENT

- Treat underlying condition (stroke, tumor, sinusitis...)
- Treat the headache itself (pain killers, triptans...)
- Stop primary headache from repeating (prophylactic therapy)




PROPHYLACTIC TREATMENT OF MIGRAINE

- Beta-receptor-blockers (propranolol)
- Calcium channel blockers (flunarizine)
- Antiepileptics (valproic acid)
- Tricyclic antidepressants (amitriptyline)
- Topiramate (Topamax)
- Serotonin antagonists
- NSAID

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NEW TREATMENTS FOR MIGRAINE

- Monoclonal Antibodies approved for the treatment of chronic migraines
 - Erenumab (Aimovig) – blocks CGRP receptor
 - Fremanezumab (Ajovy) – blocks CGRP ligand
 - Galcanezumab (Emgality) – blocks CGRP ligand

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MORE NEW TREATMENTS COMING

- Gepants -- rimegepant and ubrogepant -- are oral CGRP receptor antagonists for acute migraine treatment.
- Ditans -- lasmiditan, a serotonin 5-HT_{1F} receptor agonist for acute migraine treatment.
- Both have completed phase III trials and show efficacy -- no vasoconstriction and so will not be contraindicated in patients with vascular disease (!!!)

IN THE CASE OF HEADACHES, THE AI SYSTEM MUST NOT ONLY CLASSIFY "MIGRAINE Y/N".


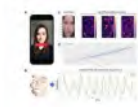
IT MUST HELP TO DISTINGUISH BETWEEN PRIMARY AND POTENTIALLY DANGEROUS SECONDARY HEADACHE.

THEN TO STRUCTURE ATTACK PATTERN, FREQUENCY, TRIGGERS, THERAPY, AND FUNCTIONAL IMPACT.

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POTENTIAL AI PROJECTS

- ✓ digital headache diary with automatic pattern analysis;
- ✓ prediction of a migraine attack based on sleep, activity, stress, time, cycle, diet and behavior;
- ✓ detection of triggers and individual patterns;
- ✓ classification of migraine, tension and cluster headaches;
- ✓ chronic migraine risk assessment;
- ✓ detection of medication-overuse headache;
- ✓ monitoring response to therapy;
- ✓ personalized recommendation of a preventive strategy;
- ✓ analysis of data from wearables: sleep, pulse, HRV, activity, temperature, stress;
- ✓ **digital phenotyping of migraine;**
- ✓ models for choosing therapy or predicting response to CGRP therapy, triptans, gepants or botulinum toxin;
- ✓ applications for the patient and doctor that visualize the course of the disease.


A PARTICULARLY IMPORTANT DIRECTION IS DIGITAL PHENOTYPING IN MIGRAINE (INCLUDES ACTIVE DATA, SUCH AS HEADACHE DIARIES AND QUESTIONNAIRES, AND PASSIVE DATA, SUCH AS SMARTPHONE AND WEARABLE SENSORS)

2025 REVIEWS HIGHLIGHT THE POTENTIAL OF DIGITAL PHENOTYPING TO CAPTURE REAL-TIME PHYSIOLOGICAL, COGNITIVE AND ENVIRONMENTAL DATA IN MIGRAINE

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POTENTIAL USE OF LLM

- ✓ taking a structured headache history and extraction of headache characteristics
- ✓ recognition of red flags from the patient's description;
- ✓ summarizing the headache diary;
- ✓ extraction of the number of days with headache per month;
- ✓ extraction of the number of days of use of acute therapy;
- ✓ identification of a possible medication-overuse pattern;
- ✓ summarizing previous therapies and reasons for discontinuation;
- ✓ preparing a summary for the neurologist;
- ✓ generation of educational material for the patient;
- ✓ explaining the difference between acute and preventive therapy;
- ✓ support in registries and clinical studies.



THANK YOU