Stages of Huntingtons Disease and Treatment

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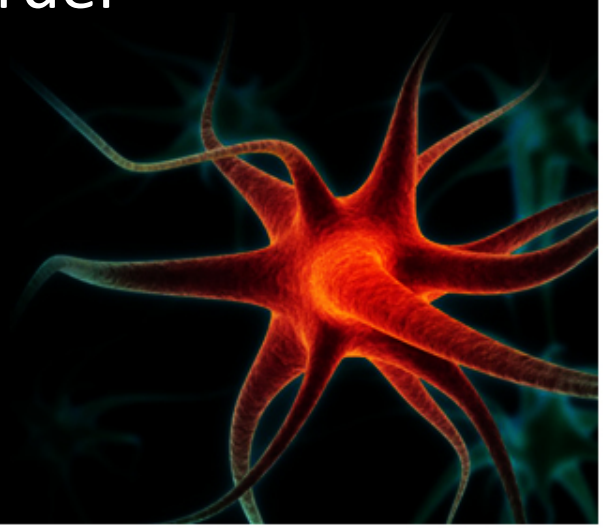
What to expect

- Overview of the stages of Huntington's disease and their symptoms
- General treatment principles
- Treatment tailored to each stage of disease

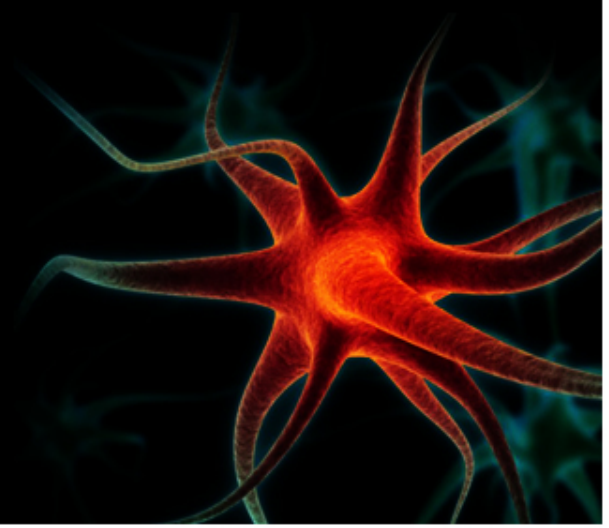
HUNTINGTON'S DISEASE

- Clinical Triad:
  - A Movement Disorder
  - A Disorder of Thinking (Cognition)
  - A Psychiatric and Behavioral Disorder



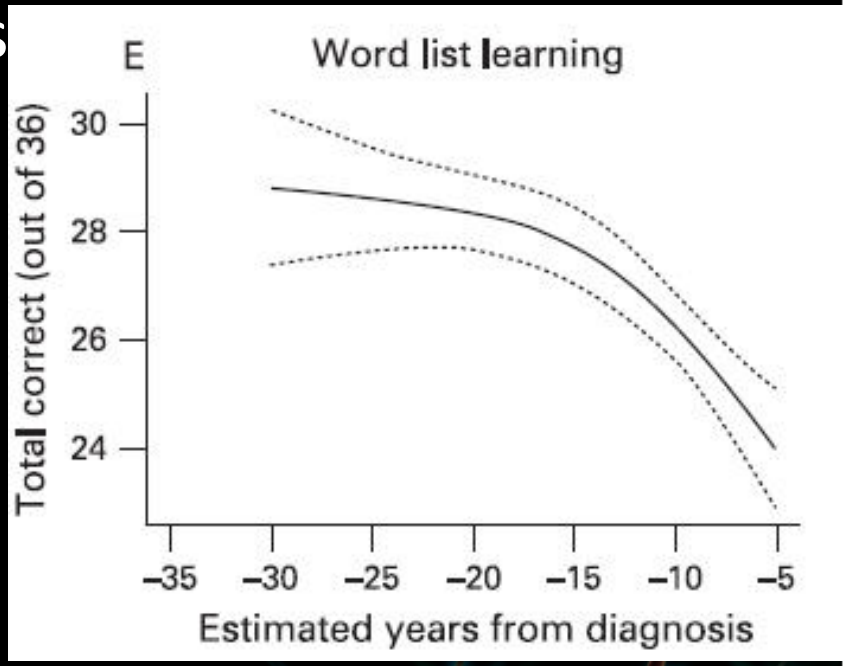
NO OBVIOUS EXTRA MOVEMENTS

PRODROMAL STAGE

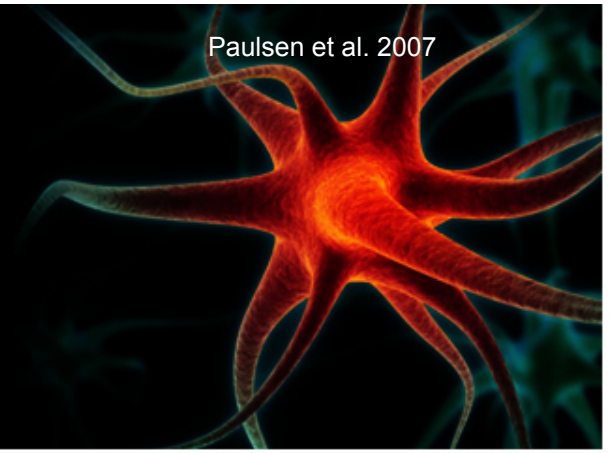


"Prodromal" Stage

- Typically no motor symptoms
- Some symptoms can occur up to 15-20 years before motor symptoms
- Cognitive changes (usually mild "executive problems")
  - Occurs in 40% of people (in 70% closer to motor onset)
  - Psychiatric changes

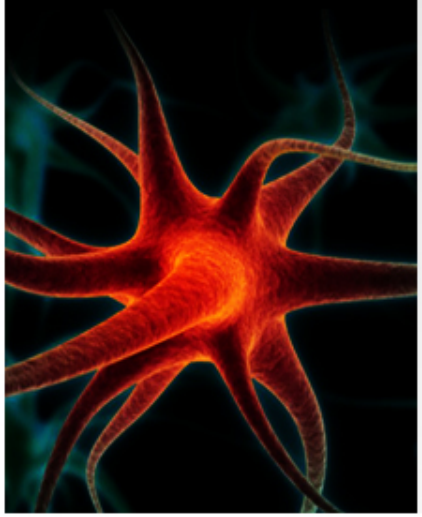


Paulsen et al. 2007



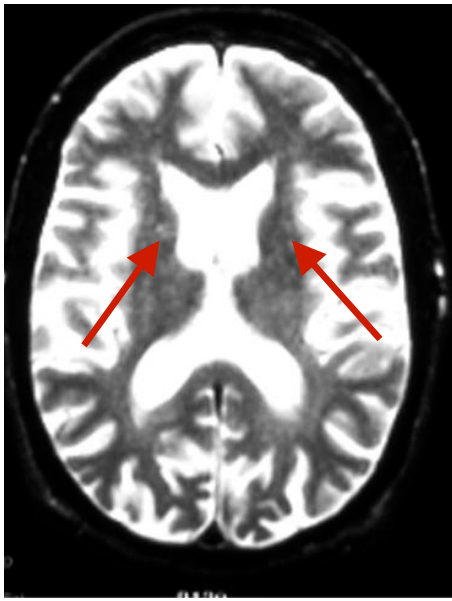
"Prodromal" Stage

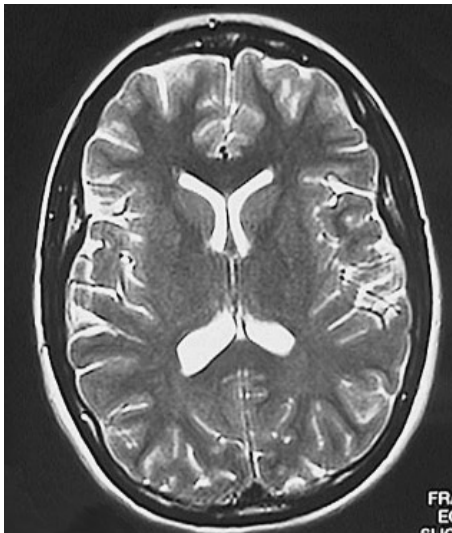
- BUT 7% of "at-risk" HD gene carriers may have motor symptoms
  - **Abnormal eye movements, changes in walking, difficulty with coordination of hands**
  - **Decreased sense of smell**
  - **Irritability and sensitivity, depression, anxiety, apathy, and occasionally psychosis**
- Symptoms can slowly increase over time until diagnosis
- Peak in suicide rate right before the diagnosis



“Prodromal” Stage

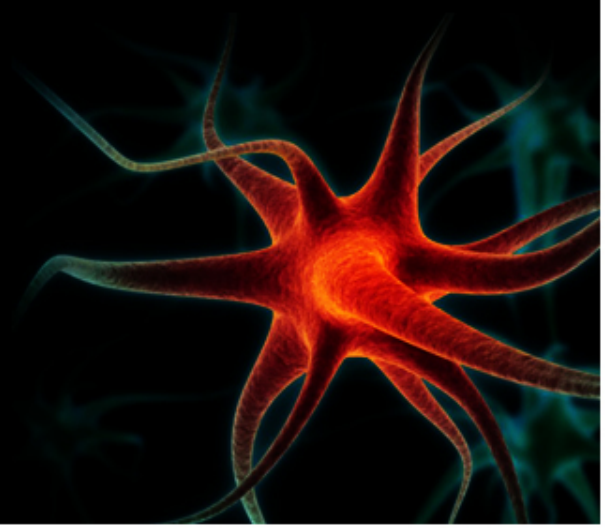
- Are there any signs the doctors can use without getting genetic testing?
  - **Subtle MRI changes 16-20 years before the diagnosis**
  - **Possible subtle cognitive changes**
  - **Could be used in the future to target therapy?**





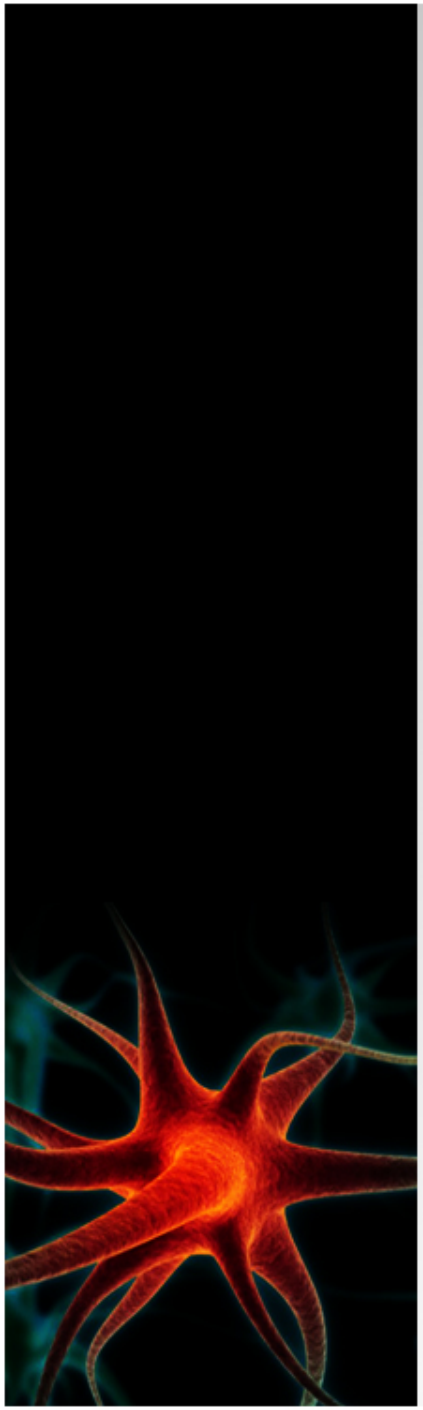
Start of involuntary movements and other symptoms

EARLY STAGE HD



Early Motor Signs of HD

- **Chorea**: continuous, irregular, and unpredictable involuntary movements that flow from one body part to another.
  - Can be confused with restlessness, agitation, or fidgetiness
  - Can sometimes suppress the movements
  - Movements can flow into purposeful actions
  - Many patients are not aware of the movements
  - Can cause incoordination or walking difficulty
  - Changes in facial expressions



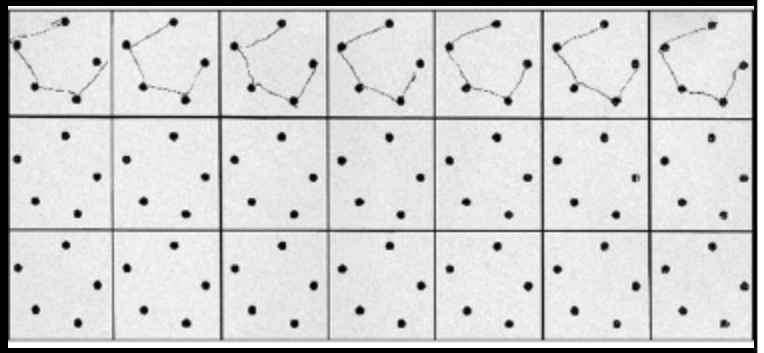
Early Changes in Mood

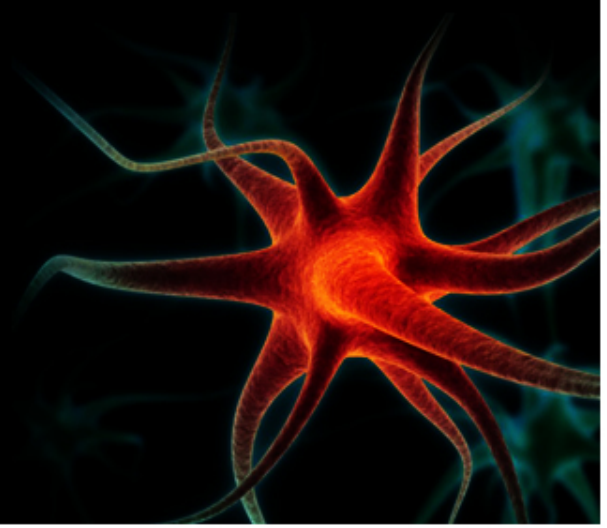
(most common early symptoms)

- ❑ Anxiety and Depression
- ❑ Irritability
- ❑ Apathy
- ❑ Impulsive Behavior
- ❑ Obsessions/Compulsions

EARLY COGNITIVE CHANGES

- Memory loss
- Executive dysfunction
  - Loss of mental flexibility, perseveration, impulsivity
  - Trouble organizing, planning
  - Slow processing speed
  - Working memory problems
  - Poor attention



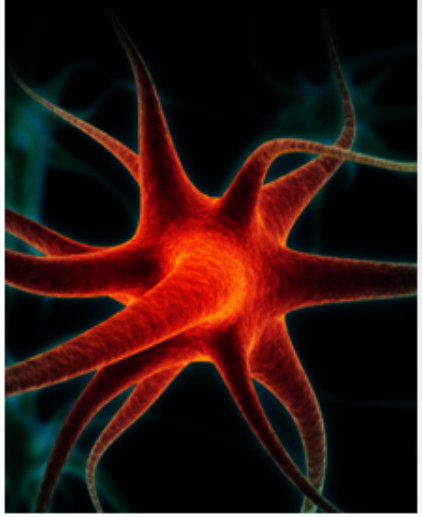


Other Early Symptoms of HD

- Speech changes
- Trouble Swallowing

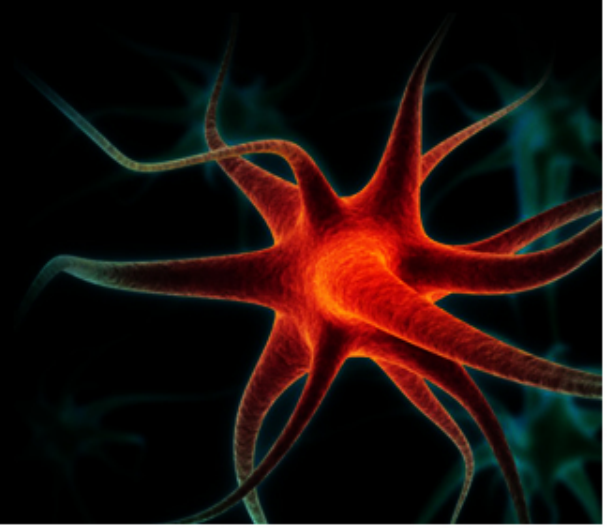
→ quickly putting food into mouth

- Non-neurologic symptoms
  - Muscle atrophy
  - Heart problems
  - Thyroid and glucose changes
  - Bone thinning and blood cell changes
- Weight loss

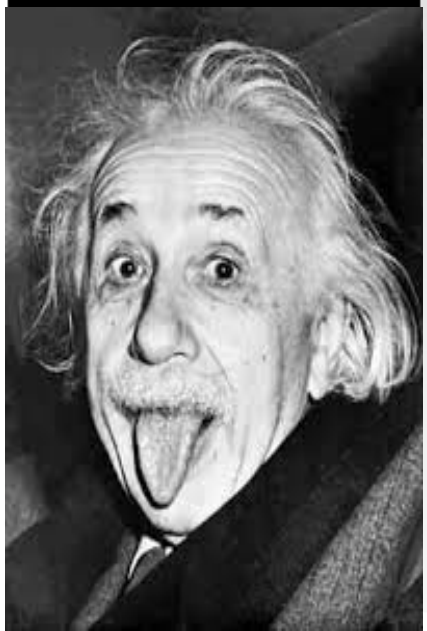


Symptoms Continue

MODERATE STAGE HD



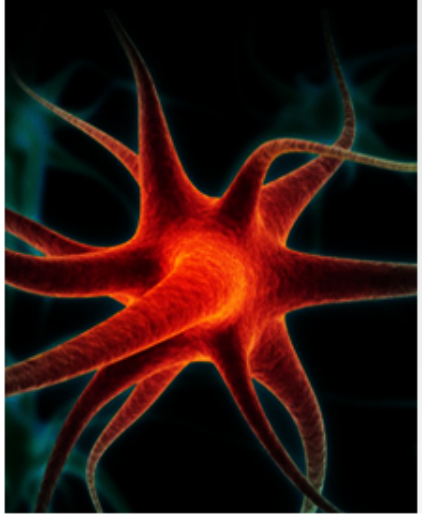
Progression of Motor Symptoms



- Worsening Chorea (not in everyone)
  - interferes with walking → can lead to falls
  - interferes with coordination → disrupts daily activities
- Difficulty maintaining action
- Speech becomes more difficult to understand → can lead to frustration
- People sometimes notice faster decline of their motor functions in these stages → adds to frustration

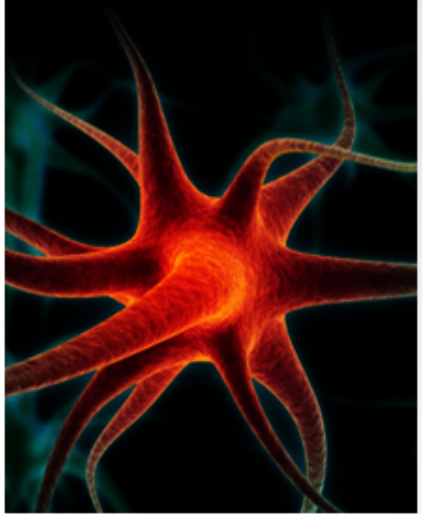
Cognitive and Behavioral changes

- Thinking becomes more impaired
  - interferes with driving abilities
  - interferes with gainful employment
- Psychiatric/Behavioral symptoms
  - Irritability
  - Anxiety
  - Impulsiveness
  - Lack of insight
- Poor sleep → worsens cognitive, psychiatric, and motor features



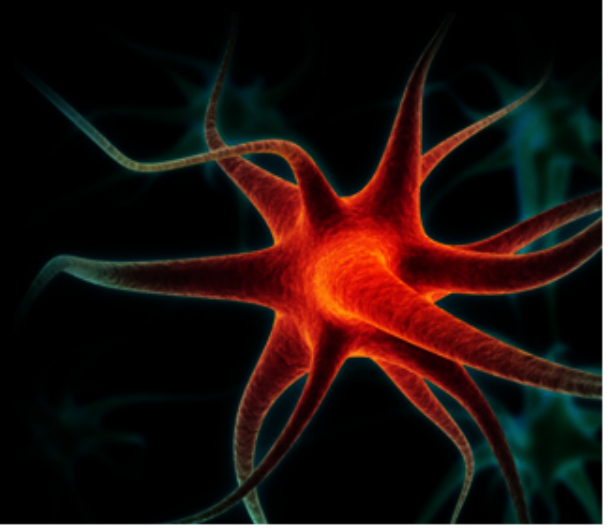
Suicide

- Second peak in suicide rates are in moderate stages
- 4 times higher than in the general population
- 3rd leading cause of death in Huntington's disease
- Loss of independence
  - Decreasing physical independence and increasing frustrations
  - Loss of driving
  - Loss of employment
  - Social Isolation
  - Family history of suicide



Symptoms Change

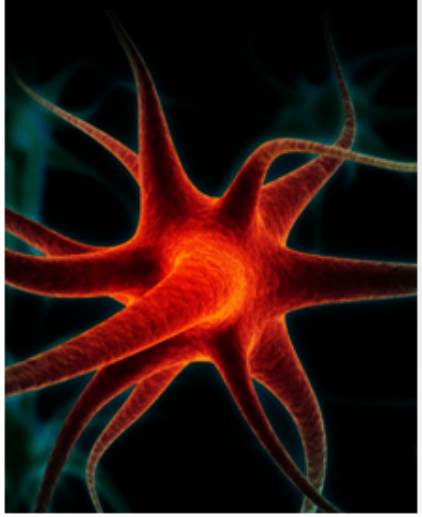
ADVANCED STAGE HD



Changes in Motor Symptoms

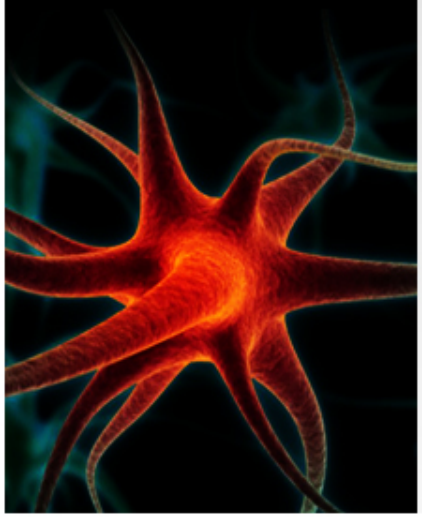
- **Chorea lessens and Parkinsonism Increases:**
  - Slowness
  - Stiffness
  - Teeth grinding, forceful eye closure
  - Abnormal limb postures
  - Parkinsonism worsened by medications
- Walking worsens
- Inability to maintain upright posture

  → increasing falls → can lead to serious injury and death



Changes in Cognition & Behavior

- Speech output becomes very difficult
- Cognition can remain the same progress
  - Processing time is increased
  - Someone with HD may just need a longer time to respond because of the speech problems
  - Always assume that someone with HD understands you
- Behavioral symptoms lessen → lower rates of suicide & aggression in this stage
- Can have episodes of significant confusion and screaming



Other Bodily Symptoms

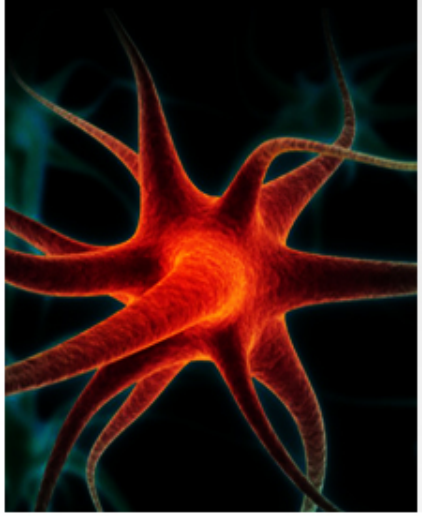
- ❑ Swallowing worsens

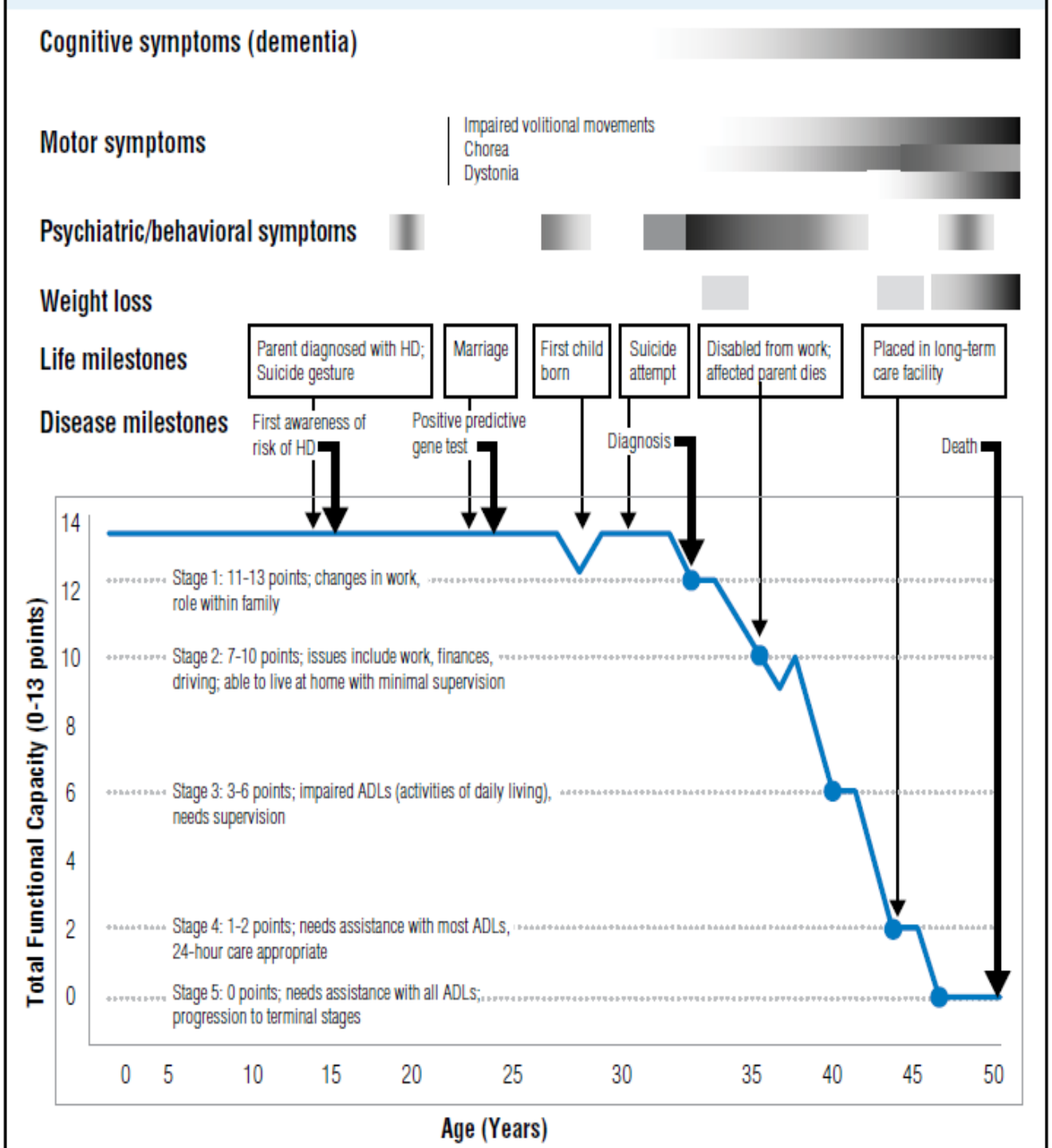
→ it may become unsafe to eat by mouth

- ❑ Physical dependence on caregivers

→ 24 hour care required for safety

- ❑ Some have severe fluctuations in blood pressure and temperature



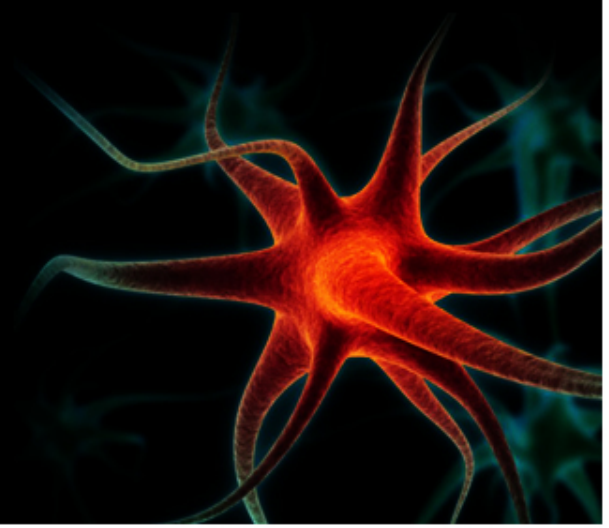


Typical Progression

A Physician's Guide to the Management of Huntington's Disease Third Edition HDSA Nance, Paulsen, Rosenblatt, Wheelock

Treatment Tailored for Every Stage

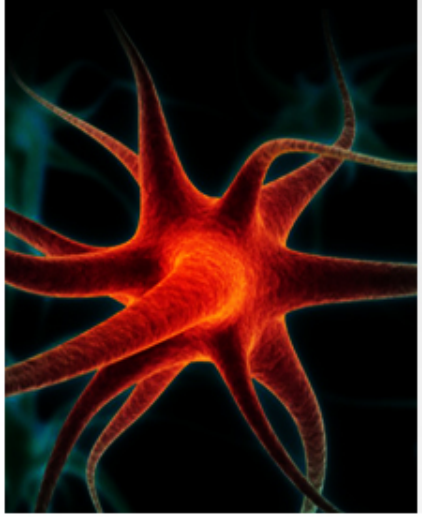
THERAPY



General Treatment Principles

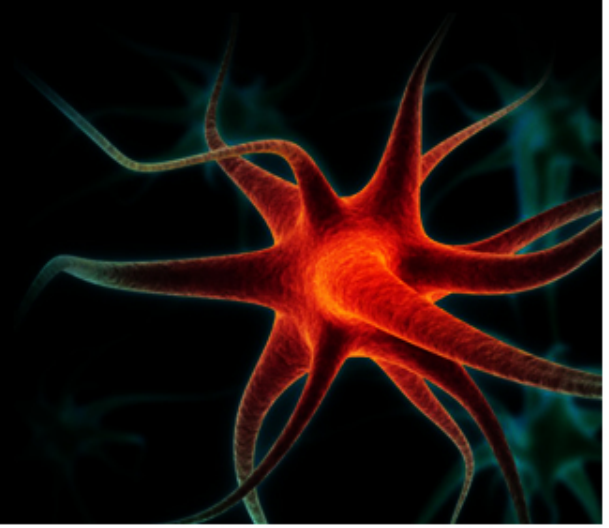
- ❑ Address all aspects of care to improve daily functioning and feel best
- ❑ Treat with medications only when needed
- ❑ Nutrition is important in all stages
- ❑ Don't underestimate "conservative therapies," such as Physical, Occupational, and Speech therapies
- ❑ Utilize psychiatric services early
- ❑ Understand that the disease makes it difficult to care for oneself for many reasons

→ Caregivers are SO important (even in early stages)



CARE IS MULTIDISCIPLINARY

- Requires caregivers
- Neurologist (coordination, medications)
- Genetic counselor
- Social worker
- PT, OT, Speech Tx, Dietician
- Nursing
- Hospice



Disease Modifying Therapies

- Currently no substance that can delay onset of disease or slow/stop the progression of disease
- What has been studied? (not comprehensive)
  - ✓ Baclofen
  - ✓ Antioxidants
  - ✓ Amantadine
  - ✓ Riluzole
  - ✓ Lamotrigine (anti-seizure medicine)
  - ✓ Remacemide (NMDA antagonist)
  - ✓ Ethyl EPA
  - ✓ Phenylbutyrate
  - ✓ Minocycline
  - ✓ **Coenzyme Q-10 (2CARE study)**
- Currently under investigation
  - ✓ **Creatine** (CREST-E Study halted for futility, unlikely PRE-CREST will have different results)

Combination Therapies

- Depakote:

→ treats Irritability, impulsivity, labile mood AND chorea and tics; Neuroleptics can also be used here (but I find less effective for mood stabilization)

- Neuroleptics (Zyprexa, Abilify, etc)

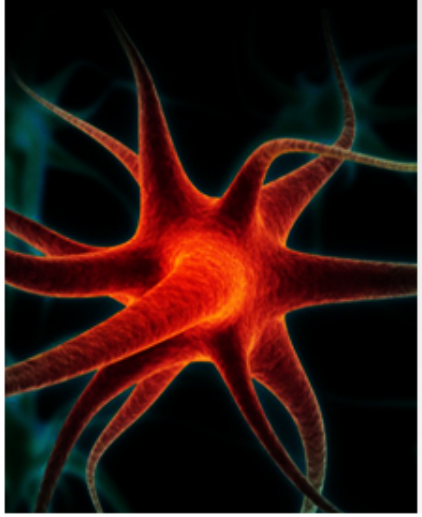
→ weight gain and anti-chorea

- Creatine:

→ weight maintenance and ? Neuroprotection

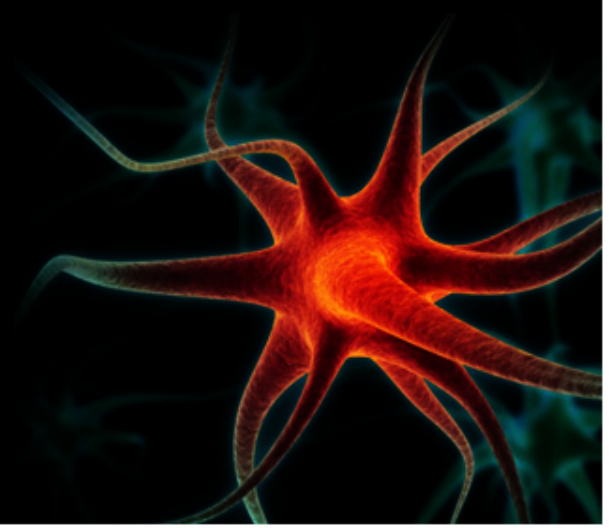
- Amantadine:

→ chorea, parkinsonism, and fatigue



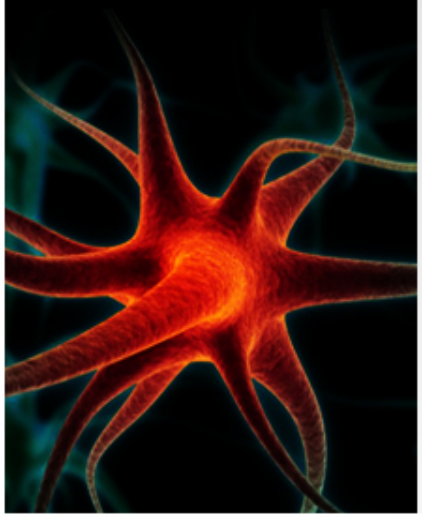
Treatment in the Early and Moderate Stages

THERAPY



Treatment of Motor Abnormalities

- **Chorea**: Do extra movements need to be treated? *Yes*... if:
  - if they are *personally* bothered by it
  - if it causes falls or injuries

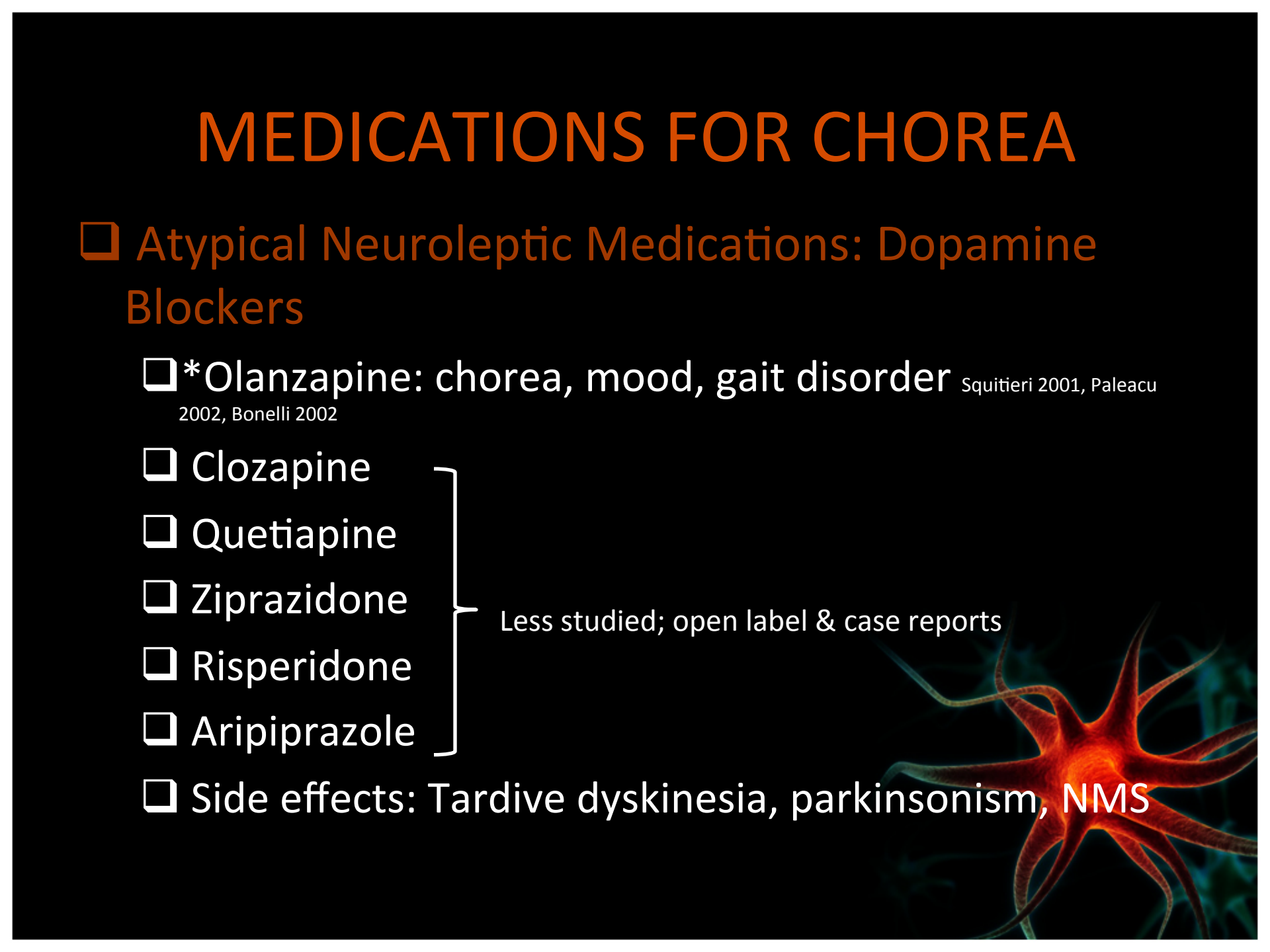


MEDICATIONS FOR CHOREA

- Atypical Neuroleptic Medications: Dopamine Blockers
  - *Olanzapine: chorea, mood, gait disorder Squitieri 2001, Paleacu 2002, Bonelli 2002
  - Clozapine
  - Quetiapine
  - Ziprazidone
  - Risperidone
  - Aripiprazole

  } Less studied; open label & case reports

  - Side effects: Tardive dyskinesia, parkinsonism, NMS



MEDICATIONS FOR CHOREA

- NMDA Receptor Antagonists
  - Amantadine (Level B)
    - 300-400mg/day, SE: hallucinations, anxiety, nausea, diarrhea
  - Riluzole (Level B)
    - 2 randomized crossover trials, no improvement at 3 years
    - 200mg/day, SE: elevated LFT's
  - Memantine
- Other:
  - Nabilone (Level C)
  - Omega-3 Fatty Acids
    - May be beneficial <45 CAG repeats (but European study found no difference)

MEDICATIONS FOR CHOREA

- Tetrabenazine
  - Dopamine depleter
  - Only FDA-approved drug for chorea
  - SE dose dependent, depression, parkinsonism, akathisia, somnolence (no tardive dyskinesia)
  - Metabolized via CYP2D6
    - fluoxetine, paroxetine use requires decrease of TBZ dose
    - May affect cardiac rhythm
  - Study found TBZ benefit chorea (UHDRS), CGI
  - Worsened some functional and cognitive measures

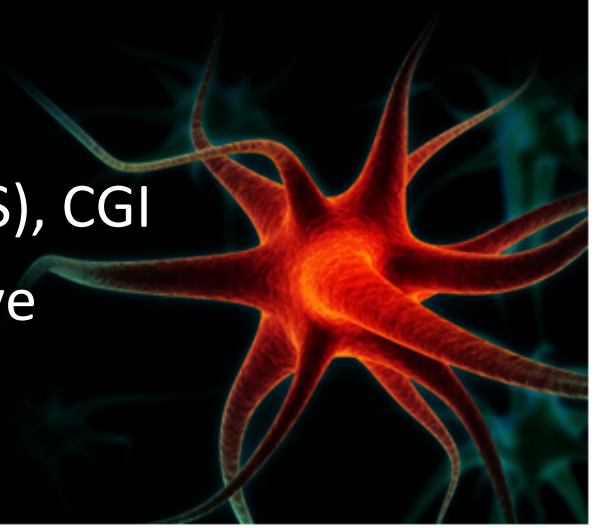


TABLE 19.4 Pharmacologic Therapy for Chore in HD

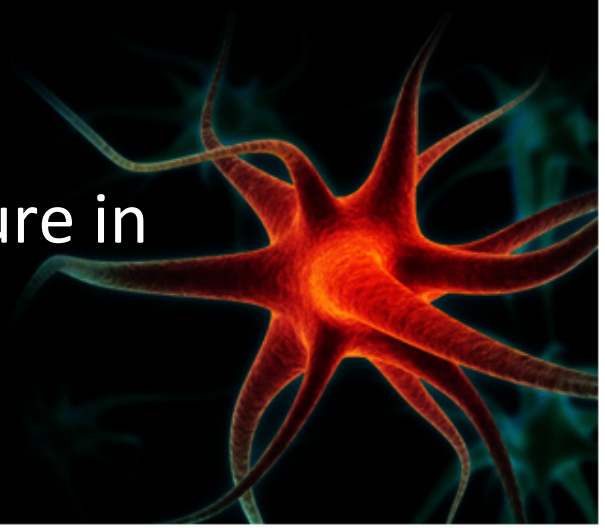
Class	Medication(s)
Dopamine depleter	Tetrabenazine
Older neuroleptics	Haloperidol, risperdone, sulpiride, tiapride
Newer neuroleptics	Aripiprazole, olanzapine
Dopamine agonists	Lisuride, apomorphine
Cholinesterase inhibitors	Galantamine, rivastigmine
N-methyl-D-aspartate antagonists	Amantadine, lamotragine, memantin riluzole
Cannabinoids	Nabilone
γ-Aminobutyric acid inhibitors	Clonazepam

MEDICATIONS FOR MOOD

- Depression
  - SSRIs are favored
- Irritability, aggression, impulsivity
  - SSRIs
  - *Atypical antipsychotics (can help chorea too)
  - Mood stabilizers

MEDICATIONS FOR MOOD

- Mania
  - Mood stabilizers
    - Lamotrigine
    - Valproic acid
    - Levitiracetam
- Apathy
  - Has not been an end point measure in treatment trial



MEDICATIONS FOR COGNITION

- Significant loss of acetylcholine and choline acetyltransferase (Spoke, Brain 1980):
  - Striatum
  - Nucleus accumbens
  - Hippocampus
- Small studies on cholinesterase inhibitors
  - Variable results

DONEPEZIL: NO IMPROVEMENT

- Open label small study (Fernandez 2000)
  - 8 patients but many dropped out from SE

- 30 patients placebo controlled trial (Cubo et al. 2006)
  - No improvement in any measures
    - MMSE, UHDRS functional, ADAS-cog, Stroop

RIVASTIGMINE MAY BE BENEFICIAL

-de Tommaso et al., 2007

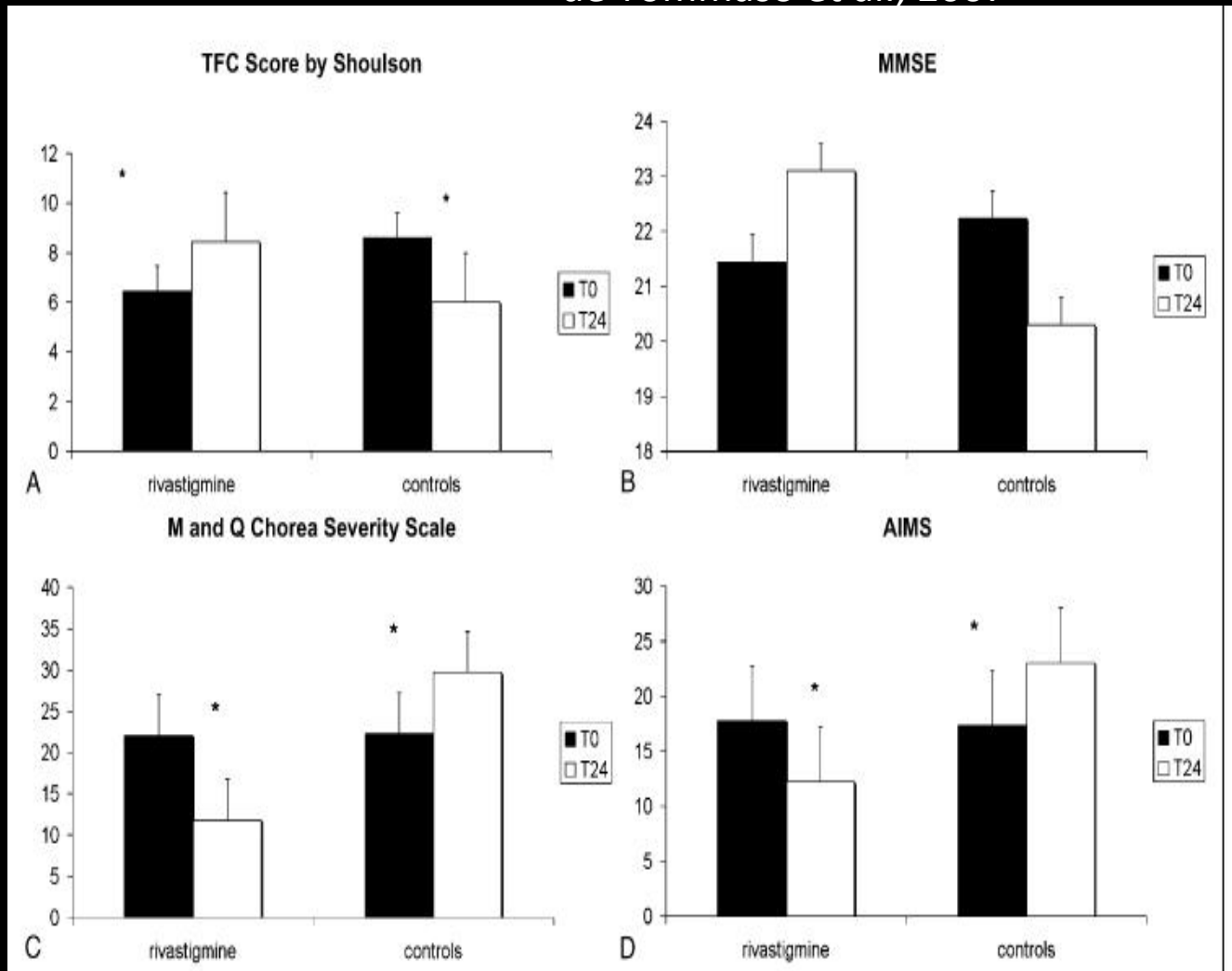
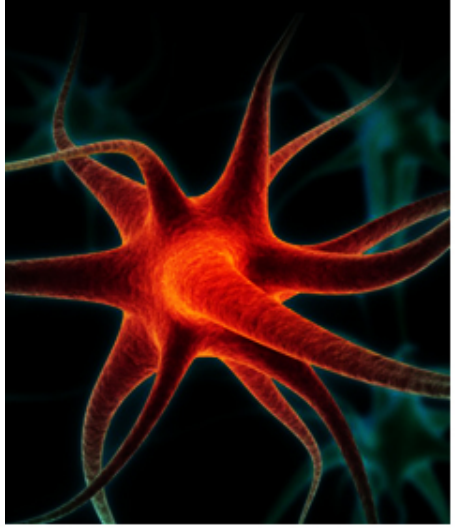
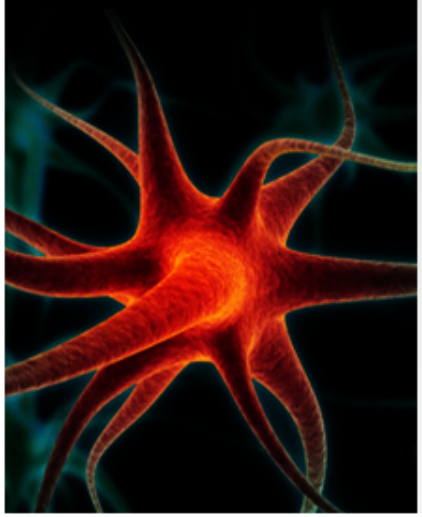


FIGURE 1. Mean values and SDs of clinical features in HD patients treated with rivastigmine and the control patients. A, TFC Score by Shoulson. B, MMSE. C, M and Q Chorea Severity Scale. D, AIMS. The results of the Student *t* test for paired data within each group are shown, $*P < 0.05$. T0 indicates basal scores; T24, 2 years' follow-up scores.



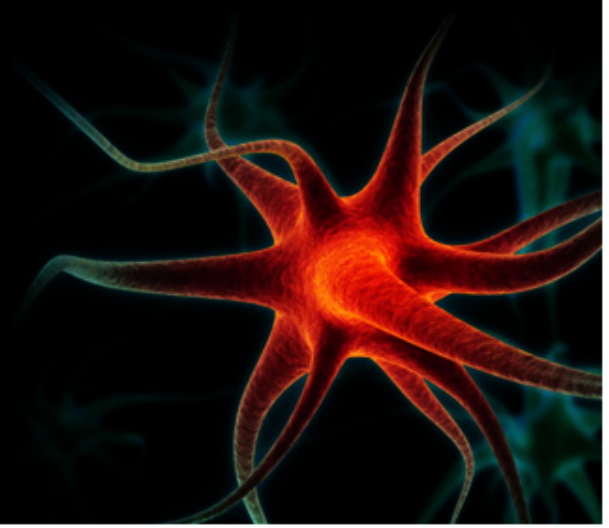
Treating other Symptoms

- Speech changes
  - Wait to finish
  - Speech therapy
- Trouble Swallowing
  - Mealtime is about mealtime
  - Small bites of food entering the mouth one at a time
  - Place down the knife and fork in between bites and take a sip of water
  - Swallow precautions
- Weight loss
  - High calorie shakes with each meal
  - Neuroleptic medications



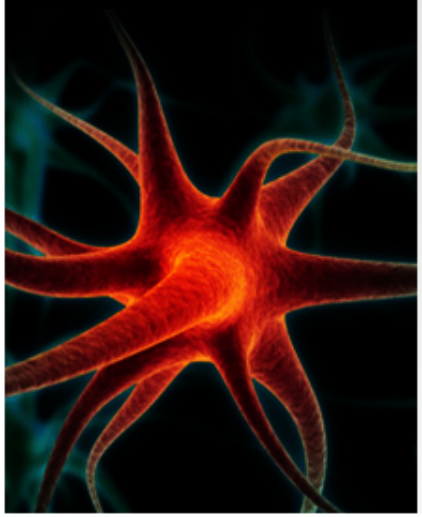
Treatment in Advanced Stage Disease

THERAPY



Changes in Treatment of Motor Symptoms

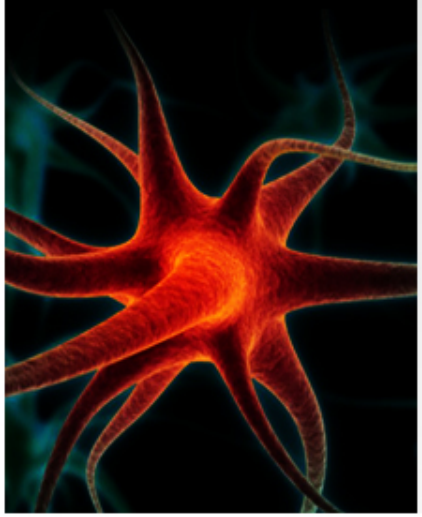
- ❑ Withdrawal of some medications
- ❑ Use of Amantadine
- ❑ Other antiparkinsonian medications



End of Life Issues

- Should be addressed **early** when patients are best able to express wishes **AND** readdressed again over time!

- Address the **"Aging with Dignity 5 Wishes" of end-of life care**:
  - The Person I Want To Make Health Care Decisions For Me When I Can't Make Them For Myself
  - My Wish For The Kind Of Medical Treatment I Want Or Don't Want.
  - My Wish For How Comfortable I Want To Be.
  - My Wish For How I Want People To Treat Me.
  - My Wish For What I Want My Loved Ones To Know.



https://www.agingwithdignity.org/five-wishes.php

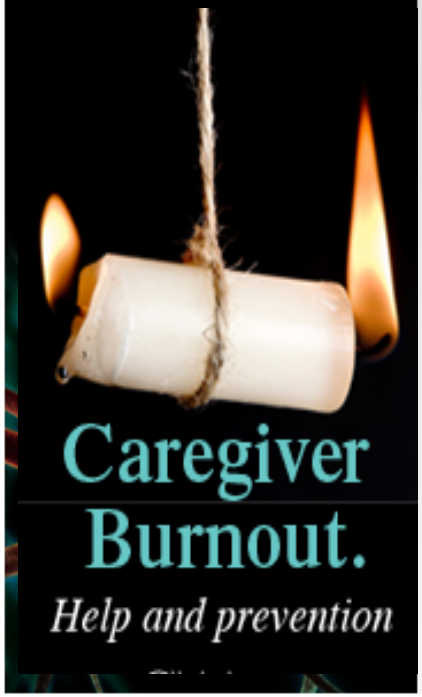
Caregiving in HD

- Emotional and Physical Demands

→ 24 hr care eventually needed

- Financial Stress (both patient & caregiver may not be able to maintain full time employment)
  - July 2012 → HD added to Compassionate Allowance Listing (CAL) to expedite disability coverage
  - Care providers living with the patient can apply for "caregiver status" (provides minor compensation for some)
- Watch for **caregiver burnout**

→ Social Work can help!



THANK YOU

Huntington's Disease Society of America
Center of Excellence

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QUESTIONS?