Terminology

- Hysteria
- Medically unexplained symptom (MUS)
- Conversion disorder
- Dissociative disorder
- Psychosomatic
- Psychogenic movement disorder
- Functional neurological disorder
Functional Neurological Disorders

• A neurological disorder, characterized by almost any type of neurological symptom, caused by a brain network dysfunction that does not exclude the possibility of normal function, sometimes due in part to a psychological cause, and not explained by other neurological pathology that may or may not be present. Symptoms may be inconsistent or incompatible (incongruent) with other known neurological disorders or human anatomy and physiology.

• Note: this is my definition as of June 2021

Somatic Symptom & Related Disorders

• Somatic Symptom Disorder
• Illness Anxiety Disorder
• Conversion Disorder (Functional Neurological Symptom Disorder)
• Psychological Factors Affecting Other Medical Conditions
• Factitious Disorder
• Other Specified Somatic Symptom & Related Disorder
• Unspecified Somatic Symptom & Related Disorder
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Conversion disorder

A. Symptoms or deficits are present that affect voluntary motor or sensory function

B. Evidence of internal inconsistency or incompatibility with recognized neurological or medical disease.

C. The symptom or deficit is not better explained by another recognized medical or DSM disorder

D. The symptom or deficit is associated with clinically significant distress or impairment in social, occupational, or other important areas of function or warrants medical evaluation.
Conversion disorder

- An unconsciously produced symptom presumably resulting from a psychological disorder.
  - The psychological disorder is converted into the symptom as a way of dealing with the disorder
  - This is the “primary gain” of conversion
  - “Secondary gains” are the benefits of being sick

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- (Malingering)
Who is referred to neurology clinics?—The diagnoses made in 3781 new patients

- Headache 19%
- Psychological/functional 16%
  - Established functional neurological disorder 5.5%
- Epilepsy 14%
- Peripheral nerve disorders 11%
- ...and so on.....

Common functional disorders

- Seizures
- Movement disorders
  - Tremor, myoclonus, dystonia, slowness, abnormal gait
- Weakness
- Sensory loss, somatosensory, visual
- Dizziness
- Speech disorders
- Memory/cognitive problems
General Principles of Diagnosis

- Inconsistency
- Incongruence
- Paroxysmal
- Distractible
- Suggestible

Functional tremor:
clinical features

- Complex movements
- Present at rest, posture and action
- Variability of frequency, direction, amplitude
- Absence of finger tremor
- Same frequency on both sides of body
- Entrainment or alteration with rhythmic tapping of another body part
- Pause in tremor produced by quick movement of another body part
- Whack-a-mole sign
- Clinical Neurophysiology can make these findings objective
What makes the diagnosis?

• The entrainment test
  – The tremor behaved like a “voluntary tremor”, not like essential tremor or other known pathological tremor
  – Frequency of tremor was inconsistent
  – Entrainment is incompatible with other types of tremor

A case of Essential Palatal Tremor

When tapping with the right 3rd finger, the palatal tremor (as measured with an accelerometer on the neck) was entrained.
Functional myoclonus: Clinical features

• Clinical features incongruous with “organic myoclonus”
  — Complexity of the movement (not simple)
  — Long and/or variable latency for stimulus induced jerks
  — Anticipatory jerks that can be demonstrated by stopping the tendon hammer just short of contact
• Exaggerated startle
• Clinical Neurophysiology
  — Bereitschaftspotential present before myoclonus
  — Stimulus induced jerks can be proven to have long latency and be variable

What makes the diagnosis?

• Jerks that are anticipatory and non-somatotopic
  — The movements are incompatible with other types of myoclonus
### Functional Myoclonus

Thompson et al. 1992

### What is the Bereitschaftspotential?

What is the Bereitschaftspotential?

Clinical Neurophysiology 117 (2006) 2341-2356

Hiroshi Shibasaki *, Mark Hallett

Ref: A1A2

Early BP Late BP

BP1 BP2

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N+50 (fpMP)

N-10 (MP)

20 μV

500 ms
A case of Abdominal Myoclonus

Functional Dystonia
Clinical Features

- Functional dystonia remains difficult!
- Many other types of dystonia have even been considered functional in the recent past
- For most cases, we just rely on general principles
- Patterns commonly dystonic
  - Fixed dystonia
  - Pulling of the mouth
  - Post-traumatic dystonia
  - CRPS dystonia
- Clinical Neurophysiology
  - Not that helpful (yet) since findings often similar to other dystonias
  - Blink reflex recovery curve useful for cranial dystonia
What makes the diagnosis?

- Facial spasms
  - The movements are inconsistent over time
  - They are incongruent with other facial spasm disorders like hemi-facial spasm

Functional Parkinsonism: Clinical Features

- Extreme slowness (sometimes with apparent great effort)
- Tremor at rest that does not improve with movement
- Sudden onset, maximum disability early
- Gegenhalten rather than true rigidity
- Laboratory: Negative DAT scan
  - Clinical Neurophysiology:
    - For the tremor: similar studies to those noted earlier

- Note that there seems to be a high co-occurrence with PD
What makes the diagnosis?

- Extreme slowness
  - The movements are inconsistent with the movements done while taking the history
  - They are incongruent with Parkinson bradykinesia
    - Movement trajectory is different with uniform slowness
    - No sequence effect
- Note also the apparent extreme effort

Gait Disorders

- Often bizarre patterns
- Some patterns are similar to, but not exactly the same, as other gait disorders; see: [Functional gait disorders](#)
  - Knee-buckling is a common pattern
- One clue is that the patient’s balance is demonstrated to be much better than claimed
What makes the diagnosis?

• Balance is better than claimed
  – Hence, incongruent with known physiology
• No apparent explanation for buckling knee
  – Further evidence of incongruence

Summary: How to make the diagnosis

• Positive features
  – It is a rule-in diagnosis, not a rule-out diagnosis

• Inconsistency
• Incongruence/incompatibility
Understanding disease

Etiology → Pathophysiology → Phenotype

Biopsychosocial model

**Biological**
- Age, Gender, Genetics
- Epigenetics
- Physiologic Reactions
- Tissue Health

**Psychological**
- Mental Health
- Emotional Health
- Beliefs and Expectations

**Sociological**
- Interpersonal Relationships
- Social Support Dynamics
- Socioeconomics
- Early life stress
- Contemporary stress

Modified from Rosen 2020 Pharos
Biopsychosocial Model

• The factors can interact
• For example:
  – Early childhood trauma can lead to changes in the developing brain, such as smaller size of the amygdala and epigenetic changes of specific genotypes, that will lead to less resilience to stress in later life and propensity to anxiety and depression, as well as the development of a FND

Sixty-eight patients with a diagnosis of FMD
• Subjects were predominantly female (73%) and Caucasian (89%), with a mean age of 46.7 years ± 8.3 [range 21–60]
• 53% reported exposure to childhood trauma
• TPH2 is tryptophan hydroxylase-2 (rs4570625)
Results

The G-703T polymorphism in TPH2 was a significant predictor of FMD age of onset

Implications of genetic study

- *TPH2* -703G/T polymorphism was associated with earlier FMD age of onset and significantly interacted with CT in predicting worse symptom severity
- The human *TPH2* gene encodes the neuron-specific enzyme isoform catalyzing the rate-limiting step in serotonin (5-HT) synthesis
- A SNP on the AADC gene, which encodes an enzyme also implicated in the synthesis of serotonin, has been associated with a greater frequency of somatoform symptoms in patients with temporomandibular disorders (Khoury et al., 2019)
Gray Matter Increases Associated with FMD

VBM in FMD

Maurer et al. Neurology 2018
Social factors

- Early life trauma
- Dysfunctional family
- Dislike of job
- Secondary gain of being ill
  - Some patients on disability, if cured, would have to go back to a job they don’t like, with an income less than what they get on disability
Understanding disease

Etiology → Pathophysiology → Phenotype
Affect processing and the right amygdala in FMD

Area of hypoactivity with functional tremor compared with voluntary mimic

TPJ = temporoparietal junction

Voon et al. Neurology 2010;74:223-228
Intention
Movement Generation
Movement Planning
Emotion
Homeostasis
Interoception
Predictive Coding
Feedback
Multimodal Integration
Agency
Loss of Multimodal Integration
Homeostasis
Interoception
Predictive Coding
Feedback
Movement Planning
Movement Generation
Feedforward Signals
Movement
Feedback
Loss of Agency
Loss of Agency
Active Inference
Active Inference
Predictive Coding
Conclusion

• Functional neurological disorders are complex, multifactorial disorders

• Etiology is best understood with a biopsychosocial model

• Pathophysiology reveals dysfunction of various networks with emphasis on limbic system and top-down beliefs

Treatment

• The first steps in treatment
  – Making the right diagnosis
  – Conveying the diagnosis to the patient
  – Acceptance of the diagnosis by the patient
Treatment Considerations

• Tell the patient what’s wrong
  – Diagnosis should be delivered as any other diagnosis
  – Show the patient how the diagnosis was made
  – “the brain itself is fine”
    • “Software problem, not a hardware problem”
    • However, this seems not completely true
  – “a brain communication/network disorder”

• Multidisciplinary treatment
  – Pharmacological
  – Psychological – CBT
  – Physical therapy/occupational therapy
  – Social work

Patients received citalopram or paroxetine; if they did not respond after 4 weeks, they were switched to venlafaxine
Table 1. Clinical outcomes at baseline (T0) and after treatment (T1) (12 weeks)

<table>
<thead>
<tr>
<th></th>
<th>T0 CBT alone</th>
<th>T1 CBT alone</th>
<th>T0 CBT + APA</th>
<th>T1 CBT + APA</th>
<th>T0 SMC</th>
<th>T1 SMC</th>
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<tbody>
<tr>
<td>Patients, n</td>
<td>11</td>
<td>10</td>
<td>8</td>
<td>8</td>
<td>29</td>
<td>29</td>
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<tr>
<td>Sex (M/F), n</td>
<td>29/0</td>
<td>4/6</td>
<td>2/8</td>
<td>2/8</td>
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<tr>
<td>Age, years</td>
<td>34.7±10.1</td>
<td>33.2±7.9</td>
<td>32.9±9.8</td>
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<td>Disease duration, months</td>
<td>17.1±12.9</td>
<td>20.7±10.5</td>
<td>19.5±11.8</td>
<td>19.5±11.8</td>
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<tr>
<td>Duration from first diagnosis, months</td>
<td>8.9±5.8</td>
<td>10.3±9.5</td>
<td>9.8±7.6</td>
<td>9.8±7.6</td>
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<tr>
<td>PMDRS</td>
<td>71.5±21.4</td>
<td>62.6±19.1</td>
<td>66.4±13.5</td>
<td>71.3±12.9</td>
<td>72.4±22.3</td>
<td>69.8±20.8</td>
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<td>PMDRS-s</td>
<td>33.2±30.2</td>
<td>28.5±27.4</td>
<td>34.2±16.7</td>
<td>72.4±22.3</td>
<td>69.8±20.8</td>
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<tr>
<td>PMDRS-f</td>
<td>8.9±3.6</td>
<td>4.6±2.9</td>
<td>9.1±1.9</td>
<td>8.3±2.2</td>
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<td>Hamilton Depression Scale</td>
<td>14.9±3.4</td>
<td>7.6±3.5</td>
<td>7.1±3.1</td>
<td>13.6±3.4</td>
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<td>Beck Anxiety Inventory</td>
<td>27.6±6.8</td>
<td>18.6±6.5</td>
<td>28.2±5.9</td>
<td>36.9±6.2</td>
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<td>PHQ-15</td>
<td>19.8±4.4</td>
<td>8.7±7.1</td>
<td>19.3±5.6</td>
<td>21.1±6.0</td>
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</tr>
</tbody>
</table>

Values are expressed as mean ± standard deviation, unless otherwise indicated. SMC = Standard medical care; PMDRS-s = motor severity PMDRS subscore; PMDRS-f = functional impairment PMDRS subscore.

* T1 vs T0 (within group); p < 0.01.
* T1 vs T0 (between groups); CBT alone vs SMC; CBT + APA vs SMC; p < 0.01.

Both groups did better than standard medical care (SMC)
Rapidity of Physical Therapy

- Balance, strength, and coordination are actually good
- Erroneous belief may well be playing role
  - If the belief can be altered, functional change may happen quickly
Other Treatments

- Psychodynamic psychotherapy
  - Mixed results
- Hypnosis: not much data
- Transcranial magnetic stimulation of motor or premotor cortex
  - Successful in some studies and ineffective in others
  - Some evidence that benefit is placebo based
- There is room for better therapies

Access to Treatment

- Can be very difficult
- Insufficient knowledgeable centers
- Insufficient knowledgeable and interested health care professionals
  - Including psychiatrists, psychologists, physical therapists
- Health care system is not really supportive either