



Neuropsychological Evaluation of ME/CFS



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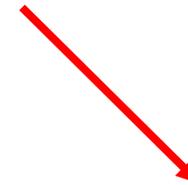
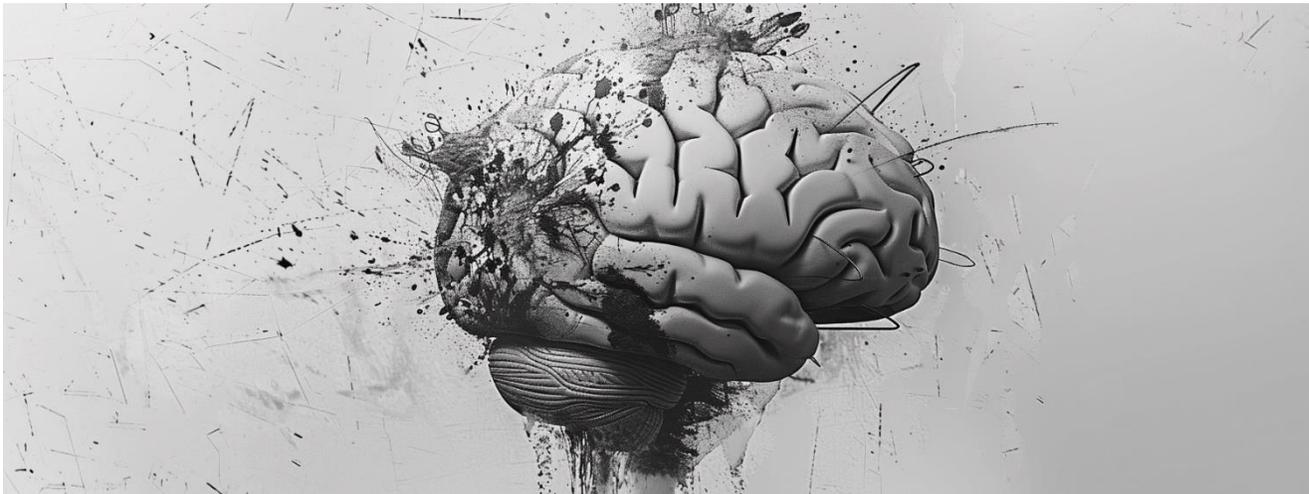
Clinical Psychologist, Health
Psychologist, Neuropsychologist

Webinar, 03/01/2024



Quick primer as a starter

***Neuropsychology** is the branch of science that studies the physiological processes of the nervous system and relates them to behavior and cognition, in terms both of their normal function and of the dysfunctional processes associated with brain damage.*



E.g.: intelligence, memory, attention, concentration, information processing, motor skills, executive functioning, language



Impaired cognition required for diagnosis?

IOM diagnostic criteria:

- ***Either*** cognitive impairment ***or*** orthostatic intolerance must be reported.
- Cognitive impairments are thus additional manifestations that might be present, but don't have to be present (thinking, memory, executive function, information processing).
- If they are present, the following frequency/intensity requirements must hold:
 - At least half of the time
 - At least with moderate intensity

Required? Not necessarily!





Impaired cognition required for diagnosis?

Canadian Consensus Criteria (CCC):

- ≥ 2 neurological/cognitive manifestations must be present:
 - Impairment of concentration and short-term memory; information processing, categorizing and word retrieval
 - Perceptual/sensory disturbances (open category; e.g., inability to focus vision)
 - Confusion
 - Disorientation
 - Motor disturbances (e.g., ataxia)
 - Overload phenomena (open category; e.g., hypersensitivity to noise)



The term „and” is usually replaced by „or”



Frequency/intensity requirements are usually added

Required? Not necessarily!



Research on the diagnostic criteria

Using the DePaul Symptom Questionnaire (54 items), a factor analytic study by Conroy et al. (2023) showed **support** for both diagnostic systems: **IOM and CCC**.

Of note:

- An independent factor „cognitive dysfunction“ emerged.
- They recommended including cognitive impairment as a mandatory criterion for IOM classification.
- About 92% reported pronounced cognitive impairment meeting the IOM threshold.
- About 96% who reported orthostatic intolerance also reported cognitive impairment.

Required? Empirically speaking: Yes!

Meta-analysis on impaired cognition and ME/CFS



Sebaiti et al. (2022) analyzed 33 studies (n = 1 086 patients/968 matched controls).

Robust impairments (at least moderate effect size) were found in:

- **Processing speed** (g between -0.59 and -0.82; e.g., WAIS symbol)
- **Attention** (g between -0.50 and -0.75; e.g., PASAT and CPT for selective/sustained attention)
- **Short term memory** (g = -0.55, Spatial Span Forward)
- **Long term memory** (g between -0.50 and -0.67; e.g., CLT, ROCF)
- **Executive functions** (g = -0.51, Stroop Test)

Is impaired cognition typical? Empirically speaking: Yes!

Interlude 1/2



Please read the following words as fast as possible

Red

Blue

Green

Yellow

Orange

Purple

Interlude 2/2



Now, please name the color the word is written in as fast as possible

Red

Blue

Green

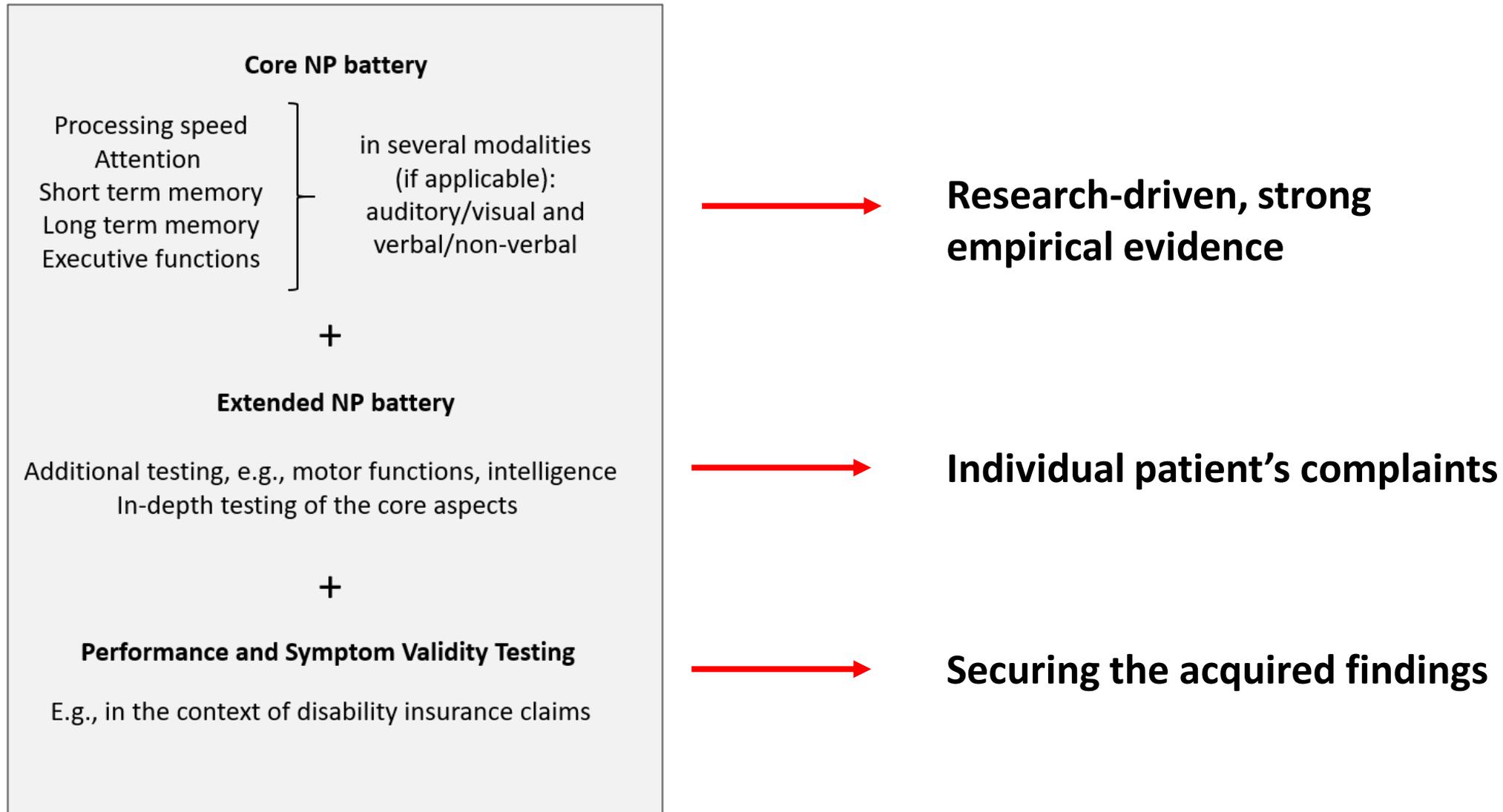
Yellow

Orange

Purple

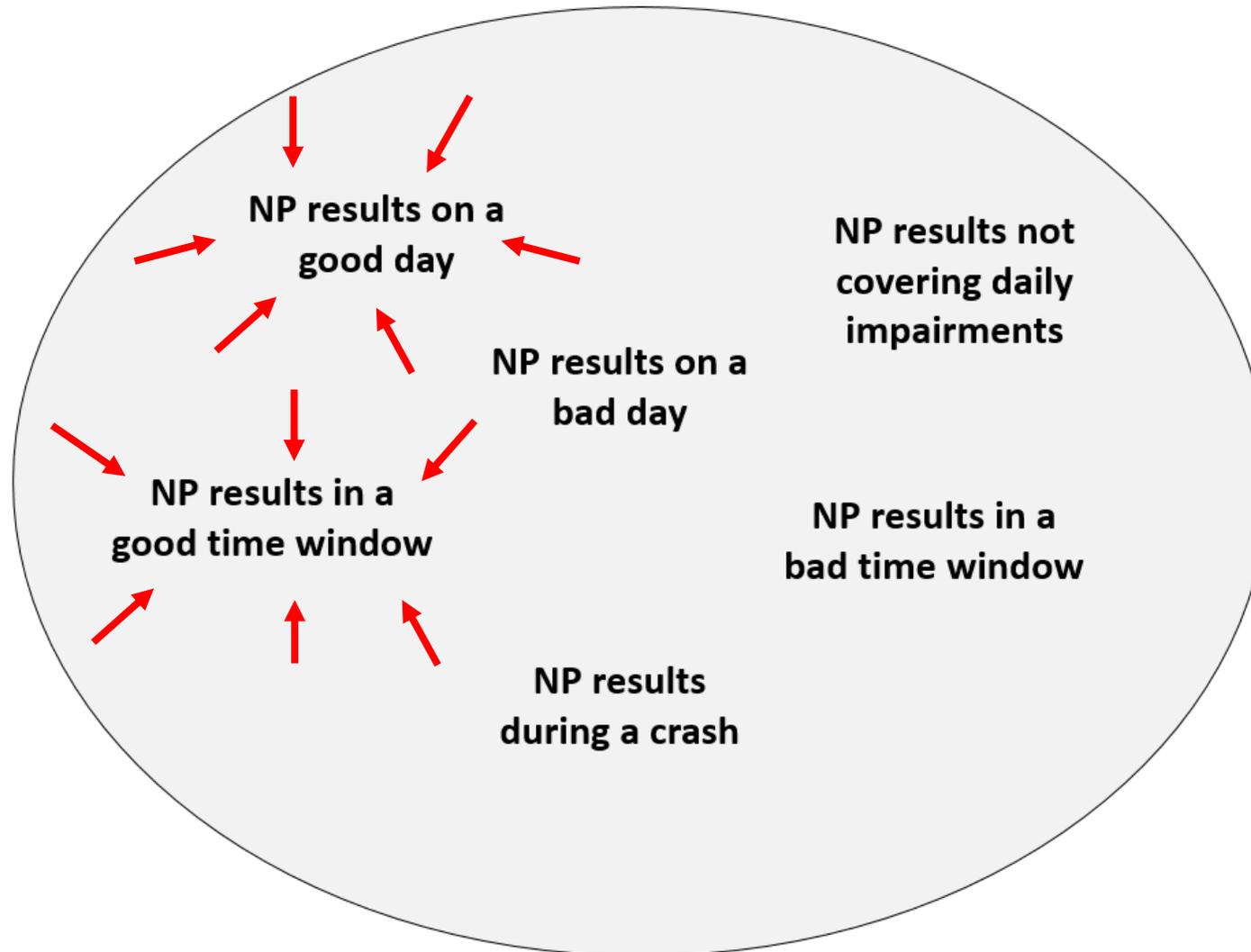


How NP testing might look like





Why NP testing alone is not enough



What about the rest?



What is still needed

The following steps help to **avoid „false negatives“** as good as possible:

Interview

Do a thorough patient history, view medical/psychological records, do a mental state examination, cover bad days



Follow-up phone call after NP testing, explore cognitive/mental post exertional malaise (PEM)



NP meets Clinical Psychology (CP)

Explain the observed impairments:

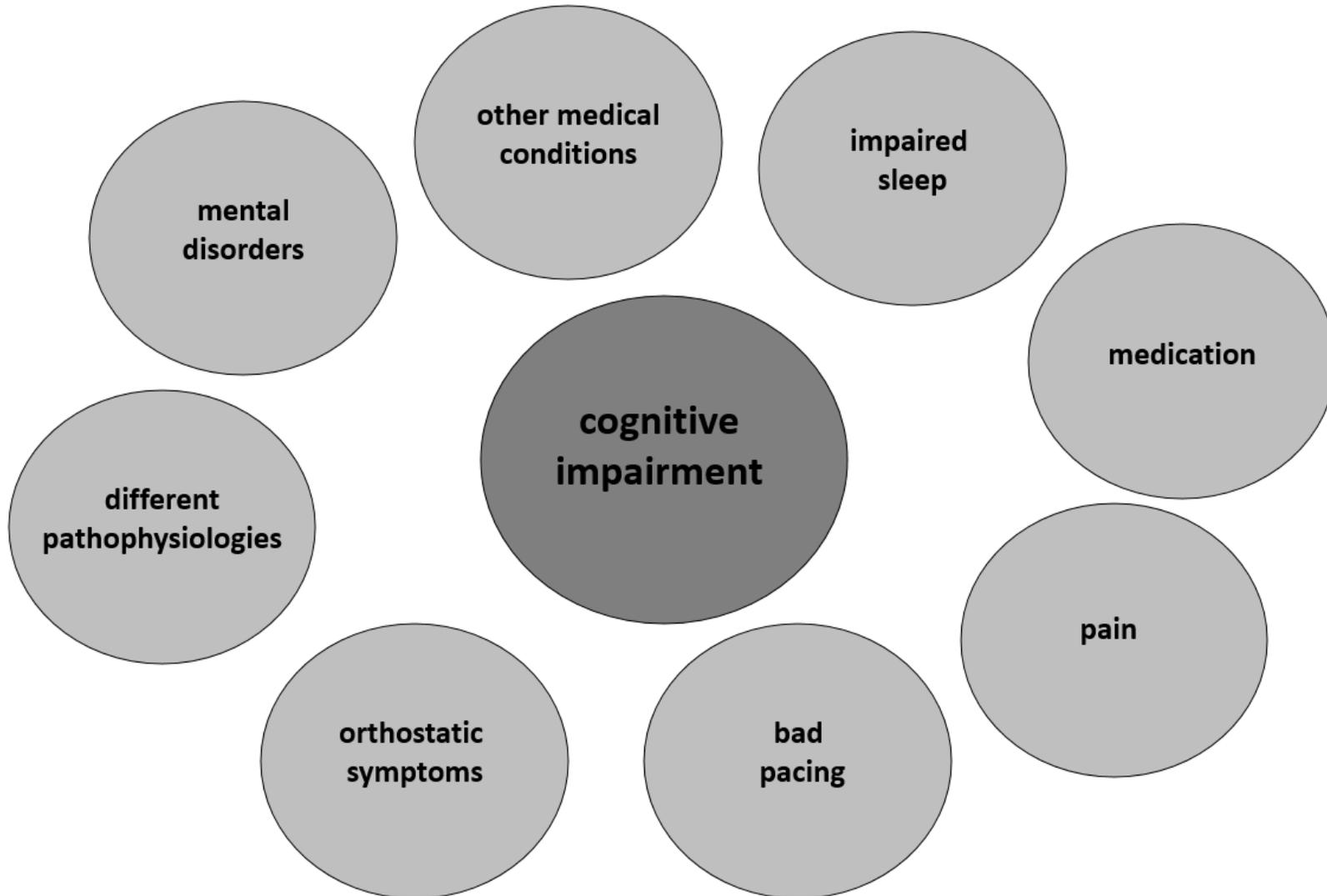
- There is no „cognitive marker“ for ME/CFS due to a lack of specificity.
- Several mental disorders share similar impairments, such as
 - Depression
 - Anxiety Disorders
 - OCD
 - ADHD
 - Schizophrenia

Consider self-report questionnaires for these variables!





Explaining cognitive impairments



**Potential contributors
and potential treatment
options**



Spotlight: neurobiological basis (1/2)

Meta-analysis of Lee et al. (2024) with more than 1 500 ME/CFS patients (65 individual studies):

- Reduced global brain activity (e.g., EEG, fMRI).
- Reduced activity in the **insular cortex** – implicated in **attention** (see also Li et al., 2021).

Function connectivity (FC) study of Inderyas et al. (2024) during the Stroop Test:

- Stronger FC between **pontine nuclei and left frontal pole/superior frontal gyrus** (responsible for **higher cognitive processes**) – hyper-stimulation due to diminished frontal activity through pontine nuclei.
- Stronger FC between regions of the **default mode network** (DMN; frontal, parietal, occipital regions, PCC) – **compensatory mechanism due to impaired cognitive functioning.**
- Self-reported **memory impairments** correlate with multiple subfields of the **cerebellum** – implicated in memory dysfunction.



Spotlight: neurobiological basis (2/2)

DTI study of Thapaliya et al. (2021), resting state:

- Diffusion deficits in the **frontopontine tract** extending to fibres of the pontine nuclei.
- Correlation of several subcortical regions in self-reported **poor information processing** (e.g., corpus callosum, hippocampus).

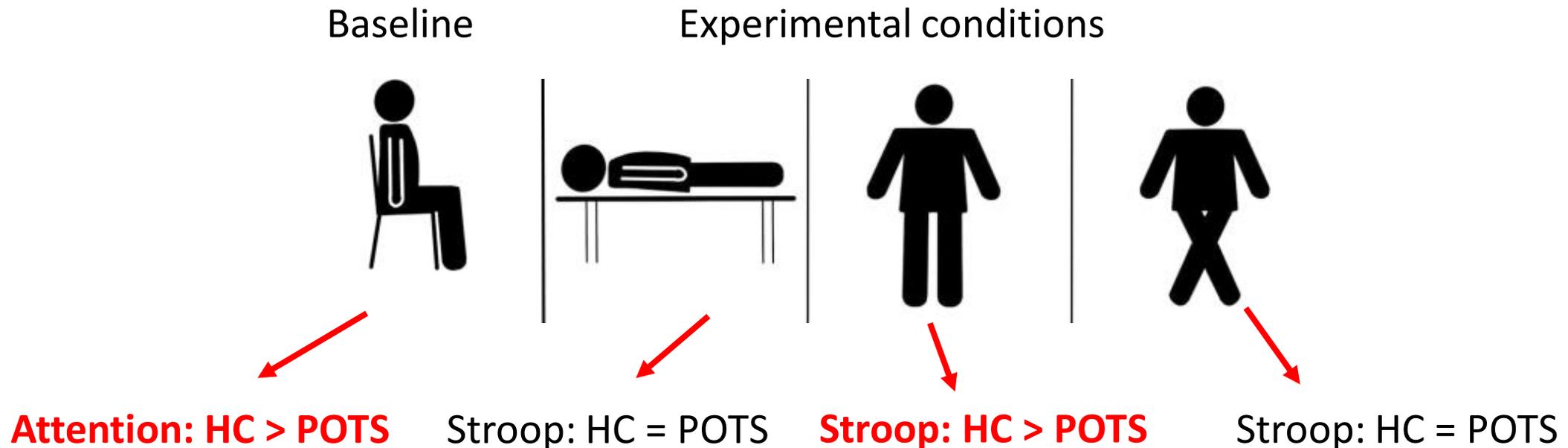
MRI studies of Thapaliya et al. (2022a,b):

- Reduced cortical thickness in parts of the **frontal lobe** (left caudal middle frontal gyrus – involved in **higher cognitive processes**) and **parietal lobe** (right precuneus – **involved in visual imagery, attention, memory retrieval**).
- Larger volumes in **hippocampal subfields** – **compensatory mechanism to maintain adequate brainstem-cortico communication**.
- Correlation between larger volumes in the **hippocampal region** and **self-reported poor information processing**).



Spotlight: POTS and cognitive functioning

Maier et al. (2023) experimentally induces cognitive impairments by varying the position.



Orthostatic stress in terms of different positions accounts for the observed differences in cognitive functioning in POTS. High comorbidity with ME/CFS!



Best practice for reaching a diagnosis

mental state examination



thorough patient history



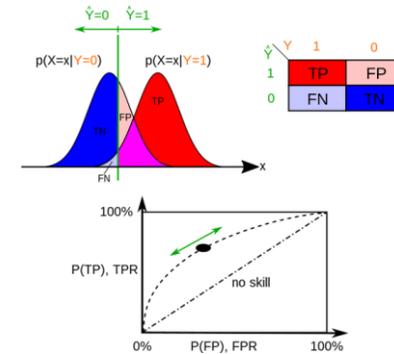
medical work-up



ME/CFS specific questionnaires



NP (and CP) testing





Thanks for your attention!

...

**... and you all passed the
Stroop Test**





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