Central neuropathic pain in MS: characteristics and mechanisms

PhD candidate: Michal Rivel

Arrow project student: Tal Gonen

Collaboration: Ruth Defrin, Anat Achiron, Gabi Zeilig

Sackler Faculty of Medicine & Sagol School of Neuroscience, TAU

Sheba Medical Center

Central neuropathic pain in MS

- Relatively frequent following CNS lesions

- Up to 30% of patients with MS

- Chronic, severe/excruciating, debilitating

- The underlying mechanism not clear

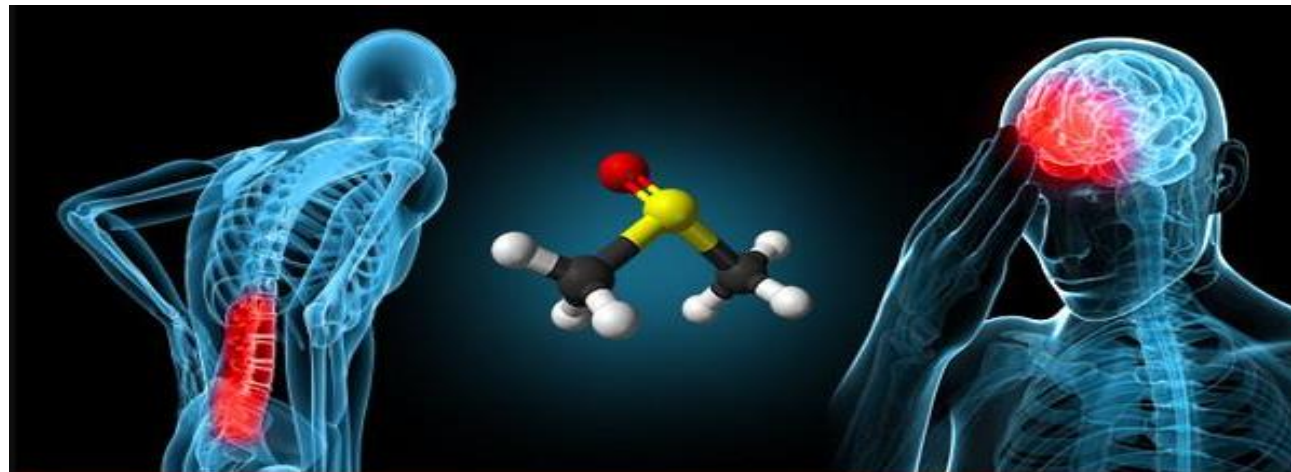- May lead to insufficient management
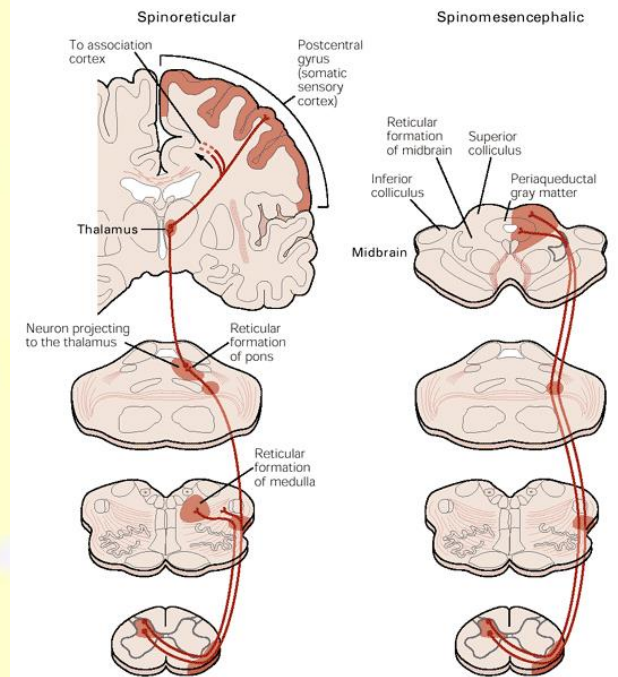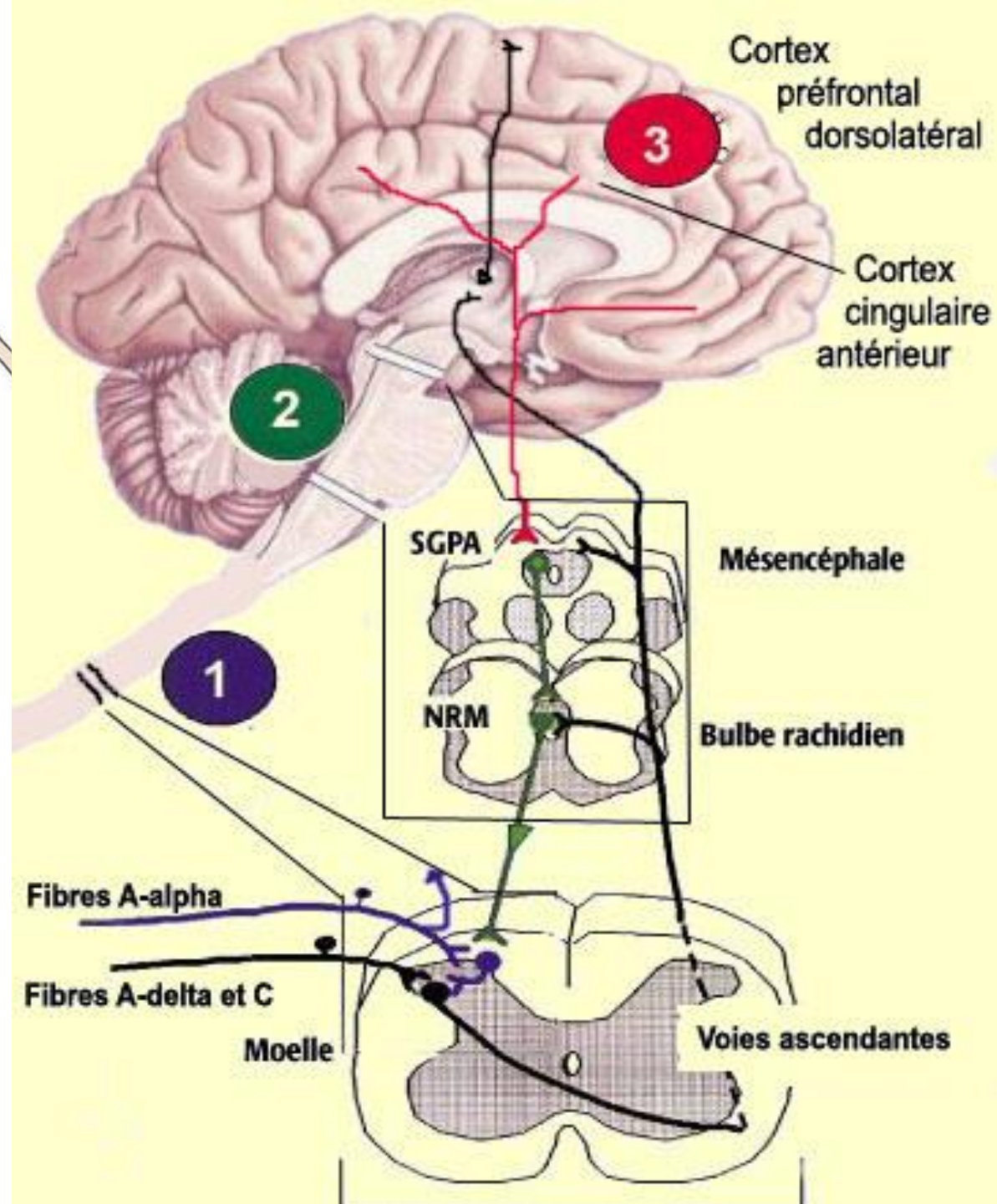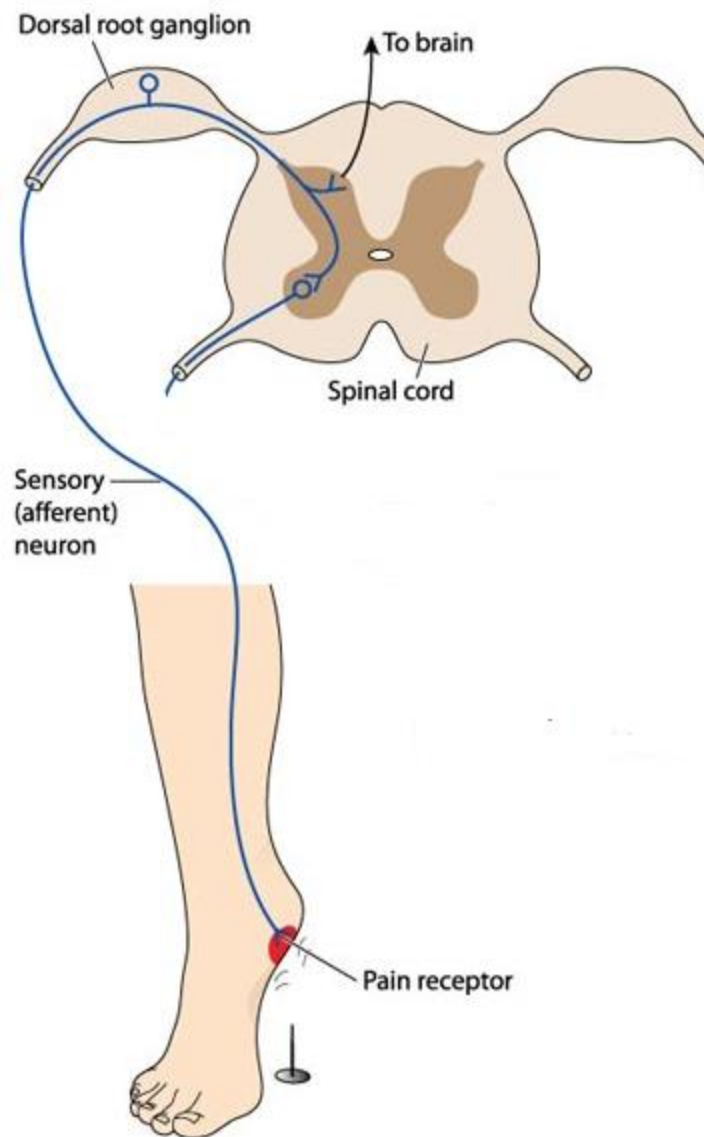
Existing information on CNP in MS is scarce

- **Only a few** studies: 3 QST studies and 2 neuroimaging studies

- **Inconclusive results** on sensory and anatomical characteristics

- **High variability** in methods, populations, tools
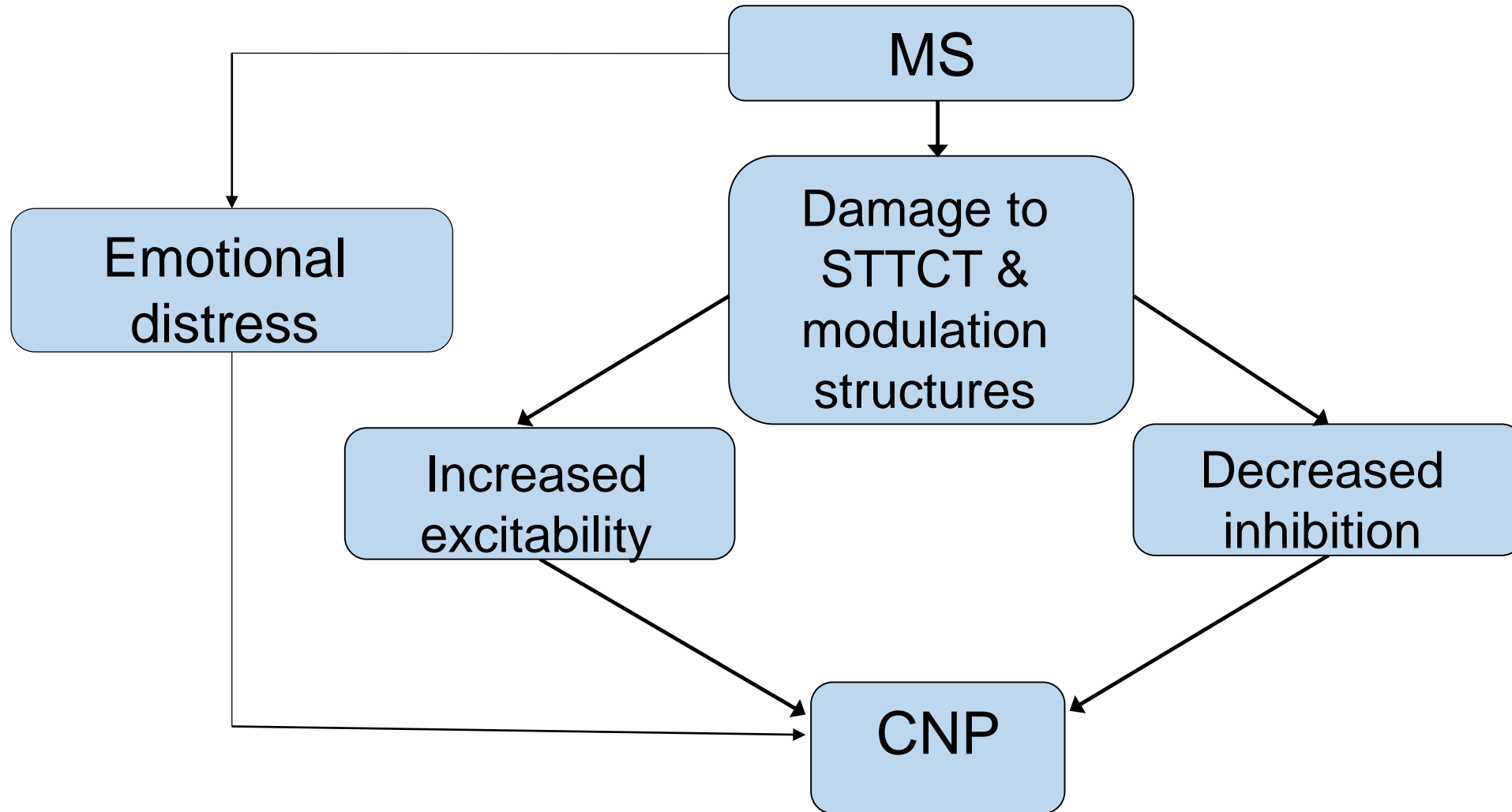
- **No follow-up** studies

Aims

1) Investigate the pathophysiology of CNP in MS

2) Search for biomarkers of CNP in MS

Dorsal root ganglion

To brain

Spinal cord

Sensory (afferent) neuron

Pain receptor

Cortex préfrontal dorsolatéral

3

Cortex cingulaire antérieur

2

SGPA

Mésencéphale

1

NRM

Bulbe rachidien

Fibres A-alpha

Fibres A-delta et C

Moelle

Voies ascendantes

Spinoreticular

To association cortex

Postcentral gyrus (somatic sensory cortex)

Thalamus

Neuron projecting to the thalamus

Reticular formation of pons

Reticular formation of medulla

Spinomesencephalic

Reticular formation of midbrain

Superior colliculus

Inferior colliculus

Periaqueductal gray matter

Midbrain

Specific aims:

1. Characterize CNP

2. Evaluate STTC, pain modulation (inhibition, excitability)

3. Characterize brain and spinal cord MS lesions

4. Study the relations between CNP-pain modulation-MS damage

5. Study the contribution of emotional distress

6. Identify early biomarkers for CNP
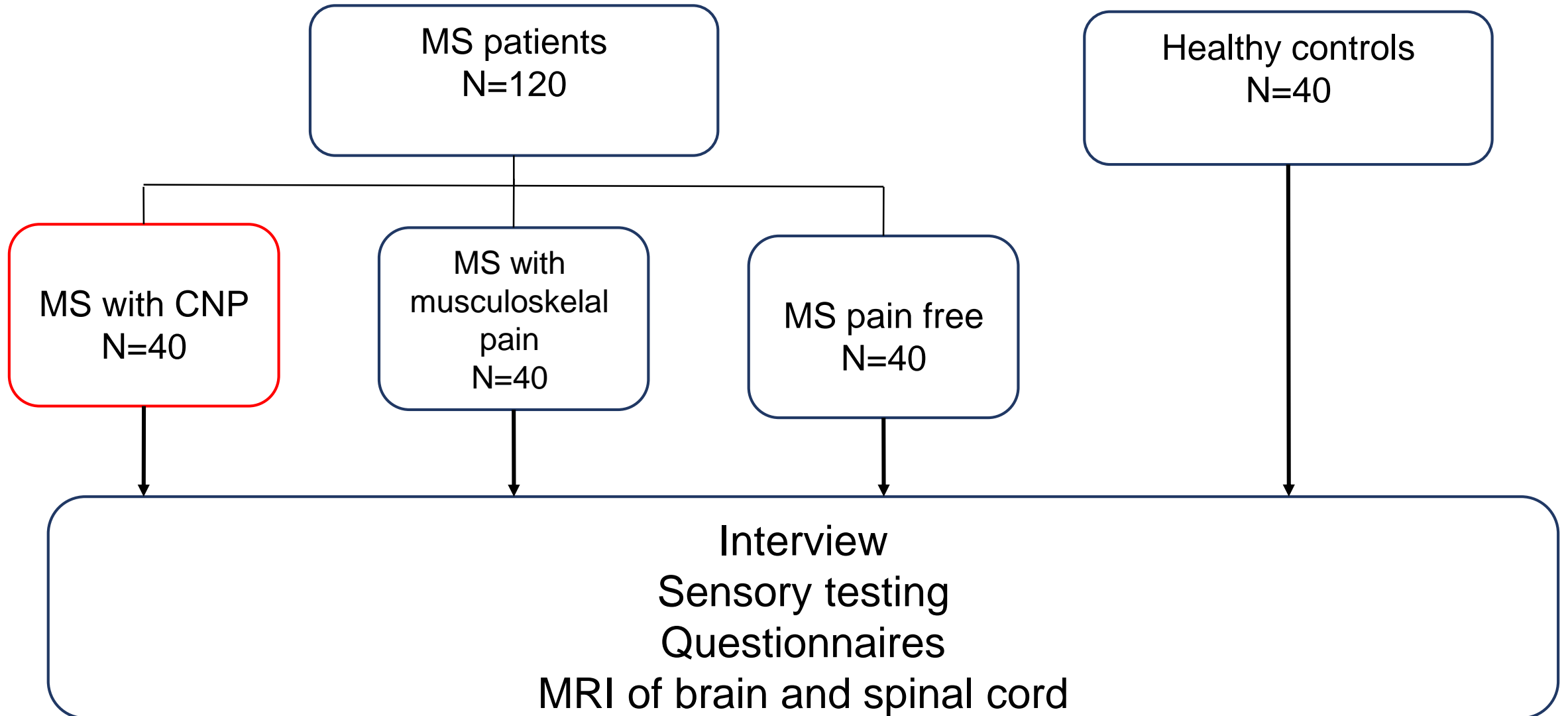
Specific aims:

1. Characterize CNP

2. Evaluate STTC, pain modulation (inhibition, excitability)

3. **Characterize brain and spinal cord MS lesions**

4. **Study the relations between CNP-pain modulation-MS damage**

5. Study the contribution of emotional distress

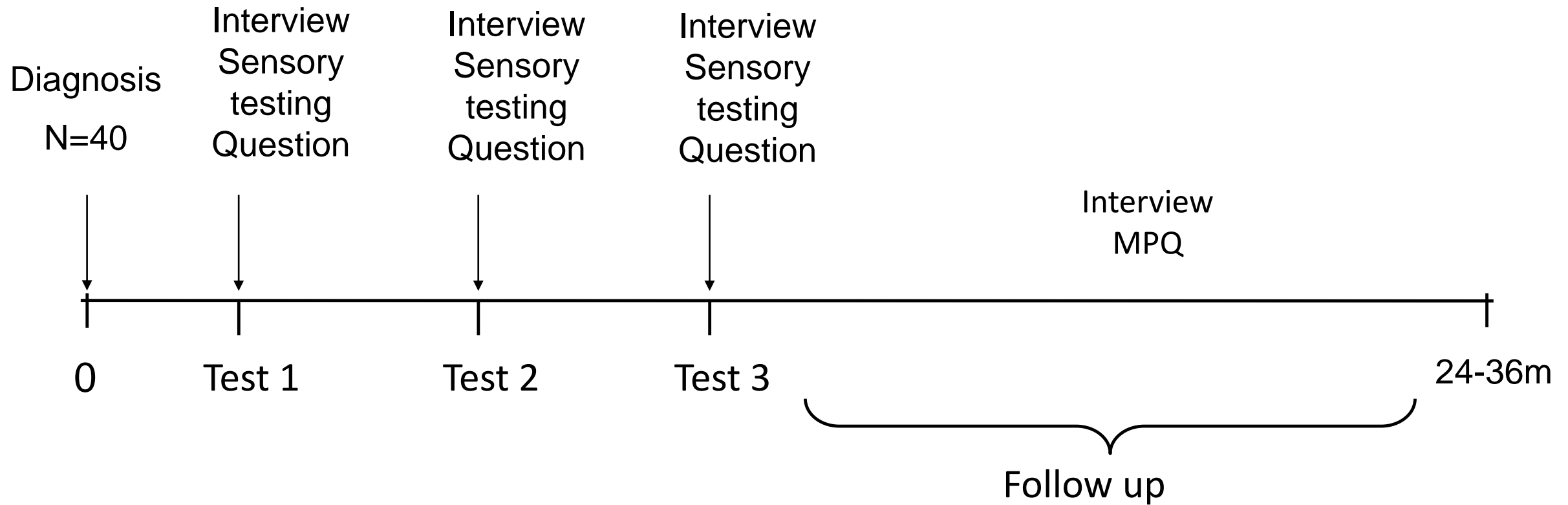6. Identify early biomarkers for CNP

Double study design:
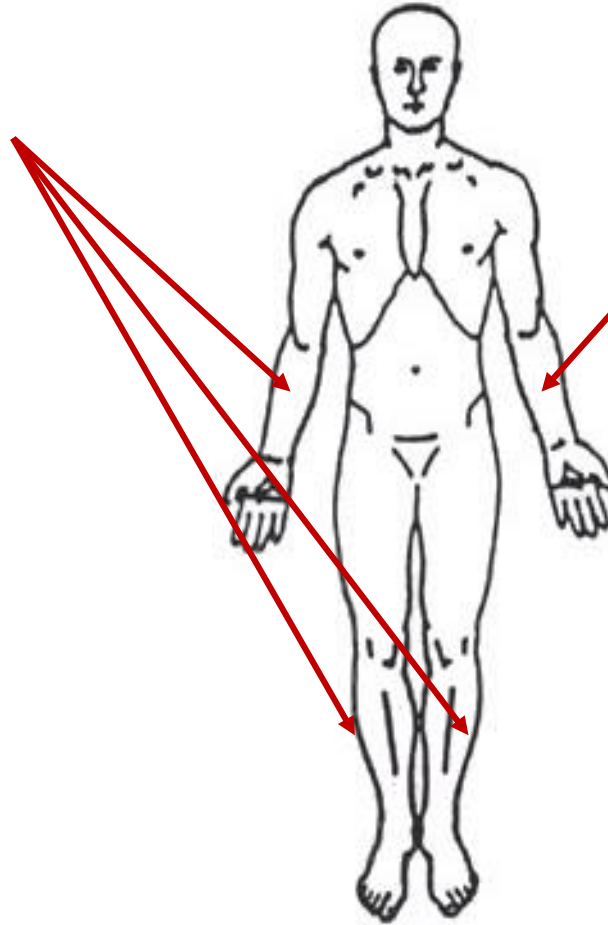
1. Cross sectional

2. Longitudinal

Cross sectional study

```
                    ┌─────────────────┐          ┌──────────────────┐
                    │   MS patients   │          │ Healthy controls │
                    │     N=120       │          │      N=40        │
                    └─────────────────┘          └──────────────────┘
```



```
┌──────────────┐   ┌──────────────┐   ┌──────────────┐
│ MS with CNP  │   │   MS with    │   │ MS pain free │
│    N=40      │   │ musculoskelal│   │    N=40      │
│              │   │    pain      │   │              │
│              │   │    N=40      │   │              │
└──────────────┘   └──────────────┘   └──────────────┘
```

```
┌────────────────────────────────────────────────────────┐
│                       Interview                         │
│                    Sensory testing                      │
│                    Questionnaires                       │
│              MRI of brain and spinal cord               │
└────────────────────────────────────────────────────────┘
```

Testing protocols

STT lesions   - warm threshold

- cold threshold

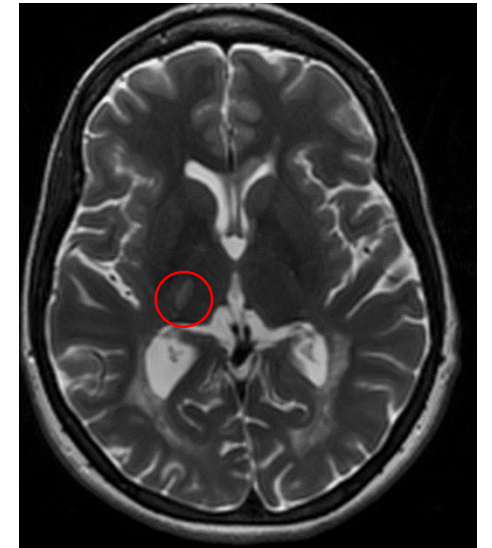- pain threshold

Dorsal lesions   -Light touch

threshold

Excitability - Temporal Summation

- Thermal Grill Illusion

- Static and Dynamic allodynia

Inhibition - Conditioned Pain Modulation

- Offset Analgesia

Questionnaires: Chronic pain (VAS, MPQ, DN4), Psychological traits
(hypervigilance, pain interference, stress, anxiety, depression, catastrophizing)