2019 Global Year Against Pain in the Most Vulnerable:

-Pain in older persons (including pain in dementia)

-Pain in infants and young children

-Pain in individuals with cognitive impairments (non dementia-related) or psychiatric disorders

-Pain in survivors of torture

Post-stroke pain- a few reminders and a blockbuster

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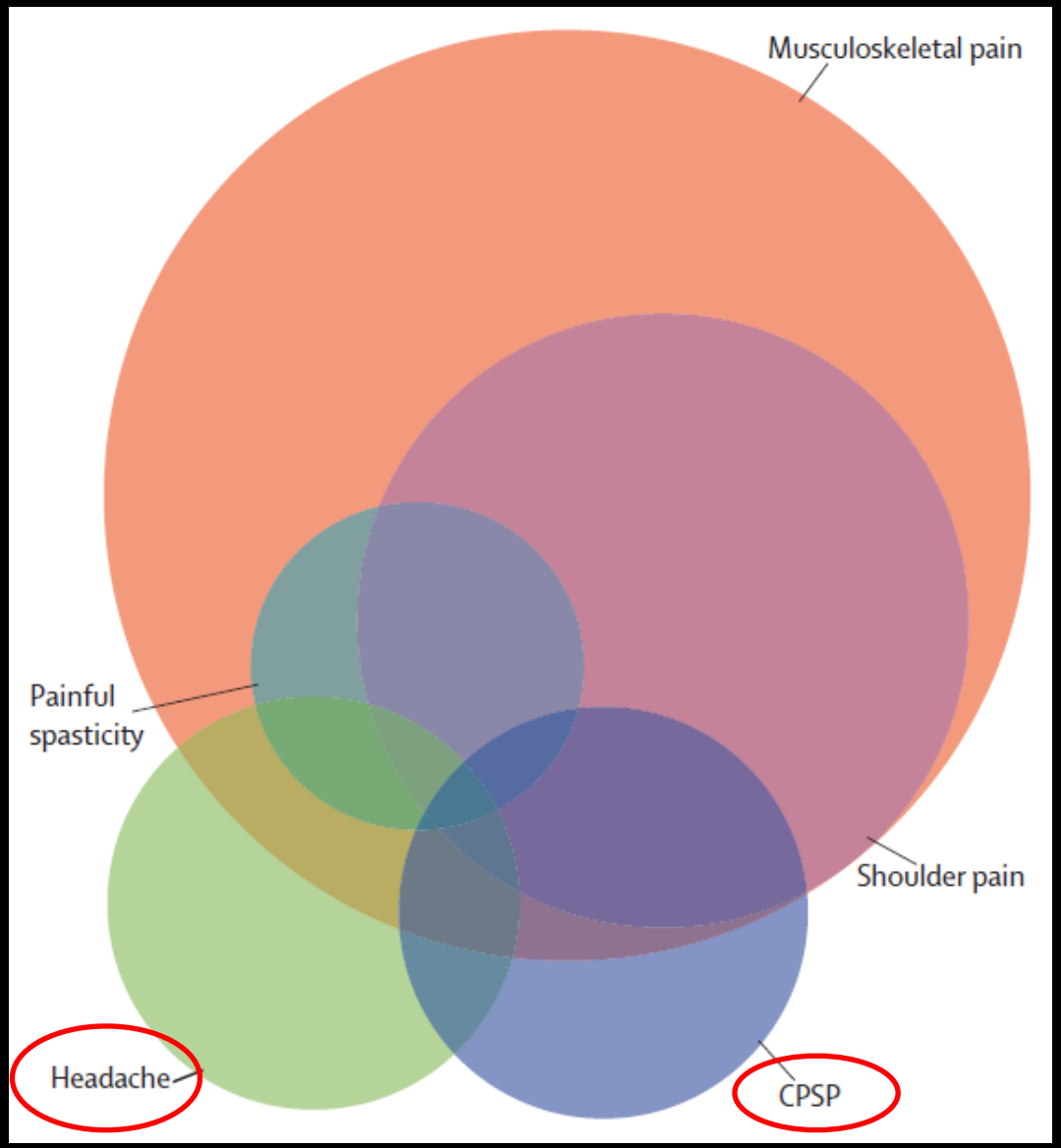
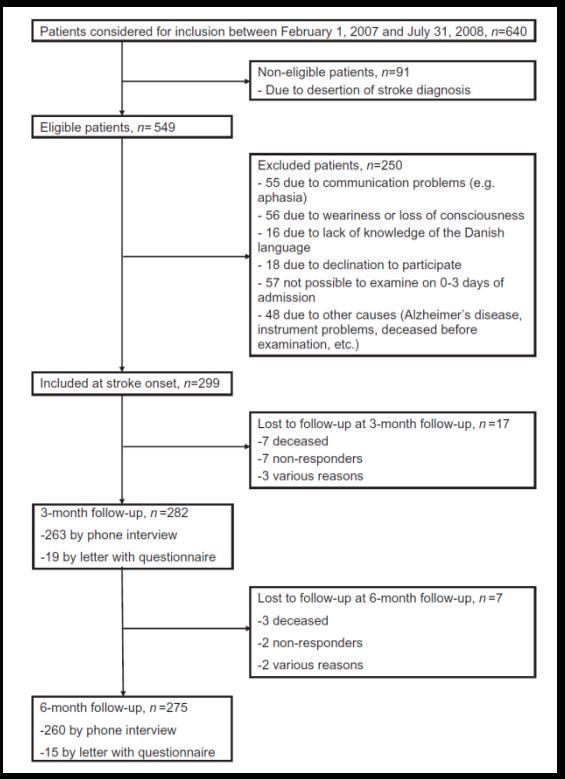
-Chronic pain after stroke in 11-55 % of patients, not always stroke related but may be pre-existing before the stroke
(Klit et al., 2009).



various combinations of one or several pain types (overlapping areas). The sizes of the circles are approximate to relative frequency (spasticity 7%, headache 10%, CPSP 10%, shoulder pain 20%, musculoskeletal pain 40%). CPSP=central post-stroke pain.



Stroke type, % (*n*/N)	
Infarct	90.5 (249/275)
Haemorrhage	9.5 (26/275)

1st interview (f-f) within 4 days after admission, phone interview at 3 and 6 months

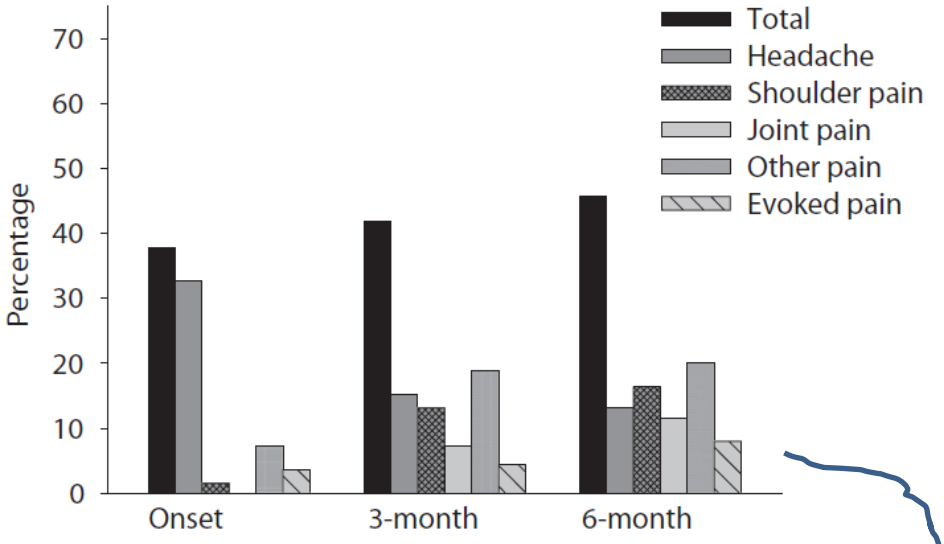


Figure 3 Incidence of newly developed pain at stroke onset and within the week leading up to the follow-up interviews.

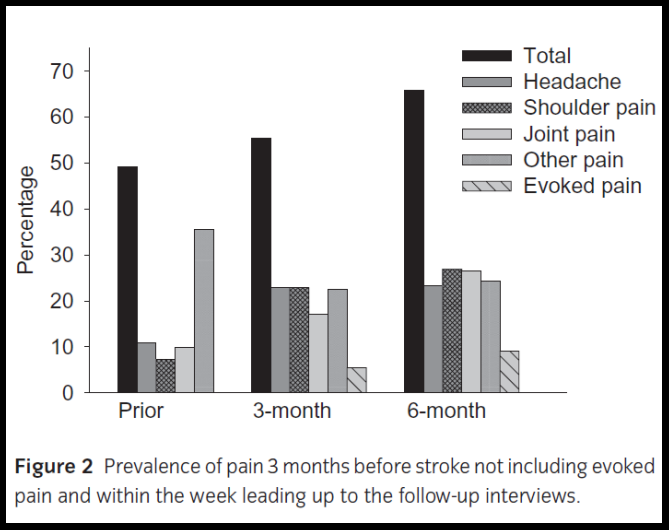


Figure 2 Prevalence of pain 3 months before stroke not including evoked pain and within the week leading up to the follow-up interviews.

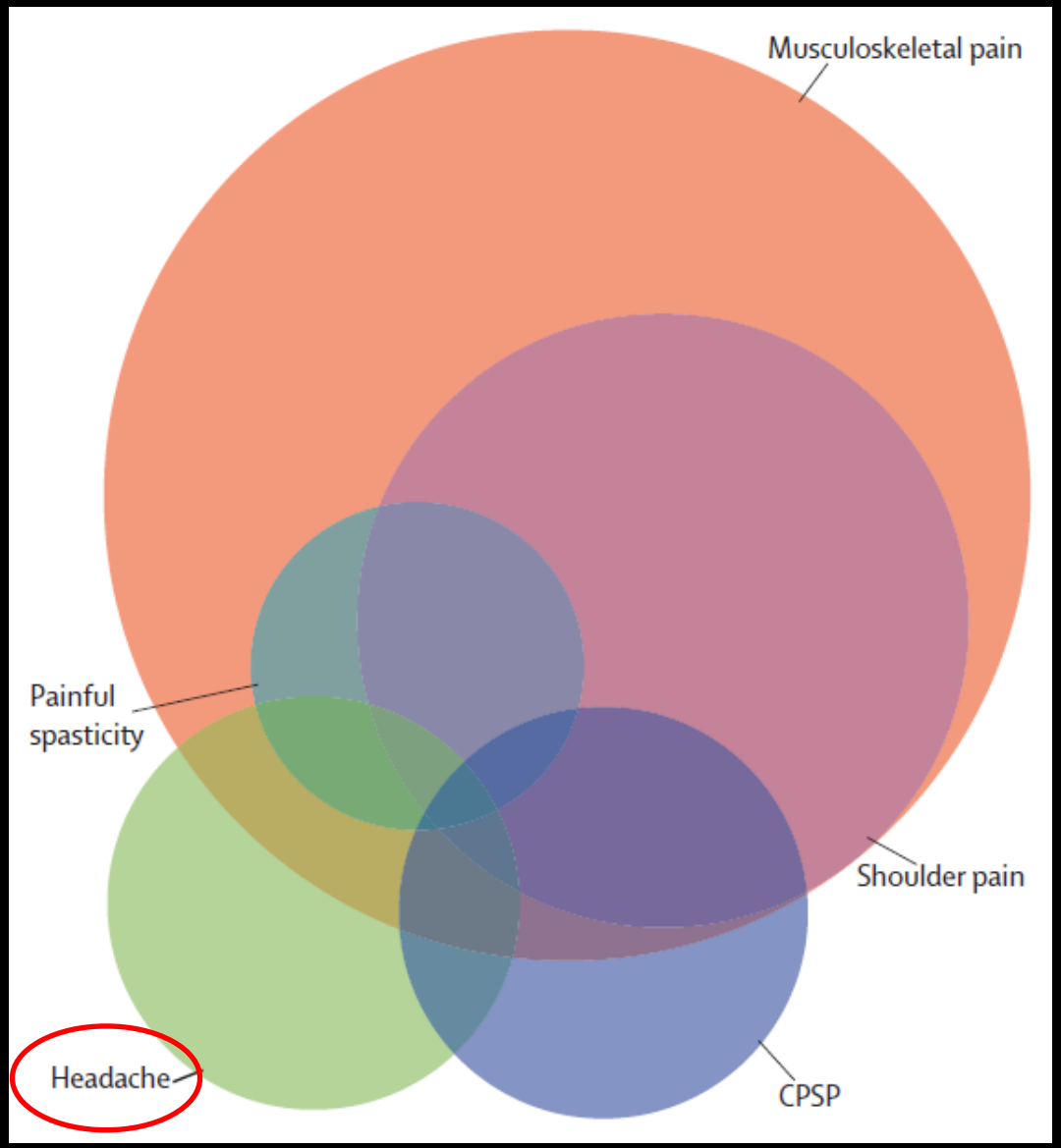
What does this study add?

- Post-stroke pain incidence of 45.8% with a moderate to severe impact on daily life in one of three patients at a 6-month follow-up.
- A distinction between different types of pain and reports on more than one type of pain in 36.5% at a 6-month follow-up.

Hansen et al., 2012

The dynamics of post-stroke pain is obvious. Implications for all physicians, nurses, physios and other health care providers:

Patients are moved to different institutions early on and different pains may come and go. Beware of the need for continuous re-evaluation and treatment changes!



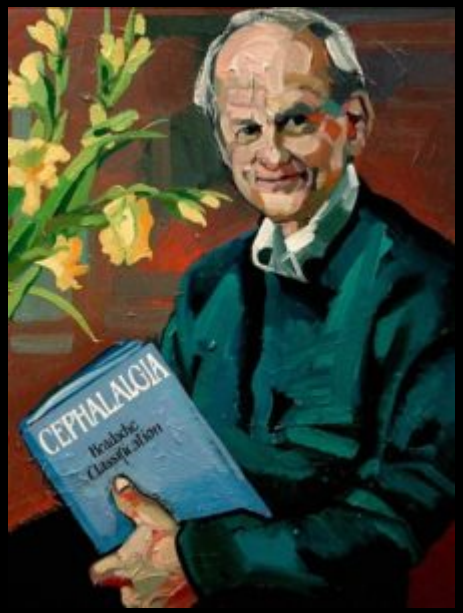
various combinations of one or several pain types (overlapping areas). The sizes of the circles are approximate to relative frequency (spasticity 7%, headache 10%, CPSP 10%, shoulder pain 20%, musculoskeletal pain 40%). CPSP=central post-stroke pain.

Klit et al., 2009

Classification

Part I: The primary headaches

- 1. Migraine
- 2. Tension-type headache (TTH)
- 3. Trigeminal autonomic cephalalgias (TACs)
- 4. Other primary headache disorders



ICHD3, 2018

Part II: The secondary headaches

- 5. Headache attributed to trauma or injury to the head and/or neck
- 6. Headache attributed to cranial or cervical vascular disorder
- 7. Headache attributed to non-vascular intracranial disorder
- 8. Headache attributed to a substance or its withdrawal
- 9. Headache attributed to infection
- 10. Headache attributed to disorder of homoeostasis
- 11. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure
- 12. Headache attributed to psychiatric disorder

Part III: Neuropathies & Facial Pains and other headaches

- 13. Painful lesions of the cranial nerves and other facial pain
- 14. Other headache disorders

Part IV: Appendix

Table 1.—Prevalence of Acute Stroke-Attributed Headache by Stroke Subtype

Stroke Etiology	Peri-Stroke Headache Prevalence Range (%)
Extracranial cervical artery dissection[1,17]	55–100
Large artery atherosclerosis[7,9,16]	15–41
Small vessel disease[12,13]	13–33
Cardioembolic[7,16]	9–39
TIA[7,10]	16–36
Intracerebral nontraumatic hemorrhage[8,10,11]	34–65
Cerebral venous sinus thrombosis[1]	80–90
Reversible cerebral vasoconstriction syndrome (RCVS)[4]	95–100

Lai et al., 2018

6.1.1.1 Acute headache attributed to ischaemic stroke (cerebral infarction), ICHD3

Description:

New and usually acute-onset headache caused by ischaemic stroke and associated with focal neurological signs of the stroke. It is very rarely the presenting or a prominent feature of ischaemic stroke. It usually has a self-limiting course.

Diagnostic criteria:
A.Any new headache fulfilling criteria C and D
B.Acute ischaemic stroke has been diagnosed
C.Evidence of causation demonstrated by either or both of the following:1.headache has developed in **very close temporal relation** to other symptoms and/or clinical signs of ischaemic stroke, or has led to the diagnosis of ischaemic stroke
2.headache has significantly improved in parallel with stabilization or improvement of other symptoms or clinical or radiological signs of ischaemic stroke

D.Either of the following:1.headache has **resolved within 3 months**
2.headache has not yet resolved but 3 months have not yet passed

E.Not better accounted for by another ICHD-3 diagnosis.

Note:The 3 months should be counted from stabilization, spontaneously or through treatment, rather than onset of the ischaemic stroke.

6.1.1.2 Persistent headache attributed to past ischaemic stroke (cerebral infarction), new in ICDH3 in 2018 (a similar included for ICH)

Description:

Headache caused by ischaemic stroke and persisting for more than 3 months after the stroke has stabilized.

Diagnostic criteria:

Headache previously diagnosed as 6.1.1.1 *Acute headache attributed to ischaemic stroke (cerebral infarction),* and fulfilling criterion C

The ischaemic stroke has stabilized, spontaneously or through treatment

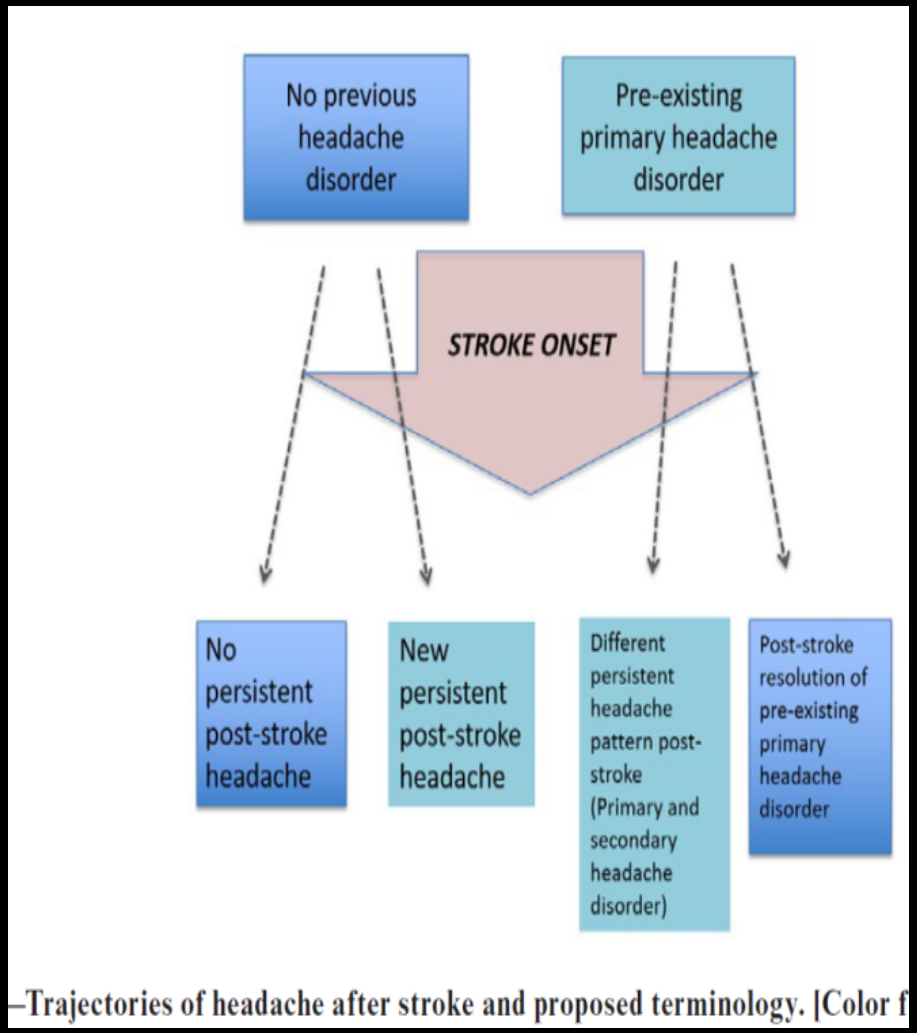
Headache has persisted for >3 months after stabilization of the ischaemic stroke

Not better accounted for by another ICHD-3 diagnosis.

Comment:

A few studies have documented headaches meeting the criteria for 6.1.1.2 *Persistent headache attributed to past ischaemic stroke (cerebral infarction)*. Research is needed to identify risk factors for such persistent headache; previous history of 1. *Migraine* may play a role, as may anxiety/depression.

Persistent post-stroke headache at 3 months after stroke?



–Trajectories of headache after stroke and proposed terminology. [Color f

Lai et al., 2018

between studies. Although patients with persistent but delayed-onset headaches after stroke are not included in this definition, it remains plausible that delayed headaches may relate to stroke. However, these patients should be reported as a separate group in future studies. We also propose standardization of the "acute" period to include 72 hours before and 7 days after stroke symptoms. "Delayed" onset headaches would then be defined as occurring more than 7 days after stroke.

Lai et al., 2018

3 types to be documented

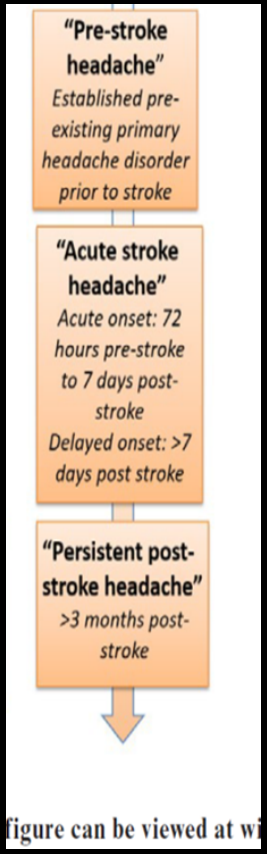


figure can be viewed at wi

Not stroke related primary headache prior to stroke.

Acute stroke-attributed headache. Same headache all the way?
Stroke-related persistent headache (new in ICHD3 in 2018).

Delayed and persistent headache (not in ICHD3).
Still may be stroke-related?

72 5 7 3

Table 2.—Prevalence of Persistent Post-Stroke Headache

Author/year	Study Design/Population	Follow-Up Period	Prevalence	Risk Factors for Persistent Headache	Headache Classification
Hansen et al (2012)[3]	Prospective cohort (n = 275) 90.5% infarct 9.5% ICH	Onset (<4 days) 3 months 6 months	Onset: 33.5% 3 months: 23% 6 months: 23.4%	Young age	Not specified
Hansen et al (2015)[2] Same cohort at 3 years	Prospective cohort (n = 222/275) 84.6% infarct 15.4% ICH	3 years	3 years: 11.7% "Stroke attributed": 61.5% "Non-stroke attributed": 38.5%	Pre-stroke headache Right-sided stroke Lack of atrial fibrillation	Tension: 50% Migraine: 31.3% Mixed: 7.7% Med overuse: 3.8% Other: 3.8%
Klit et al (2011)[21]	Retrospective population-based survey (n = 608 stroke patients/1127) Stroke type unspecified	Median follow-up: 794.5 days Range (588–1099)	Follow-up period: 10.5% vs 2.3% (reference population	Young age	Not specified
Naess et al (2010)[22]	Prospective cohort (n = 408) 80.4% infarct 12.5% TIA 7.1% ICH	Median follow-up: 372 days Range (185–757 days)	Follow-up period: 10.8%	Younger age Female sex Post-stroke fatigue Pain in paretic limb	Not specified
Jonsson et al (2006)[23]	Prospective cohort (n = 297) 89.2% infarct 6.4% ICH 4% SAH 0.3% undefined	4 months 6 months	4 months: 7% 6 months: 10%	Headache-specific risk factors not reported	Not specified
Melo et al (1996)[11] – cohort at onset Ferro et al (1998)[14] – same cohort at 2 years	Prospective cohort (n = 289 a onset, n = 90 at 2 years) 100% ICH	Onset 2 years	Onset: 57% 2 years: 11%	Female sex Pre-ICH headache Depression	At 2 years: 20 patients with new tension type headache, 1 patient with new migraine headache

Tension type and migraine.

Lai et al., 2018

Table 3.—Risk Factors for Persistent Post-Stroke Headache

Risk factors for persistent post-stroke headache
Demographic
• Younger age
• Female sex
Clinical
• Pre-existing headache disorder
• Headache at stroke onset
• Stroke mechanism: Dissection, cerebral venous thrombosis
Psychosocial
• Post-stroke fatigue
• Post-stroke depression

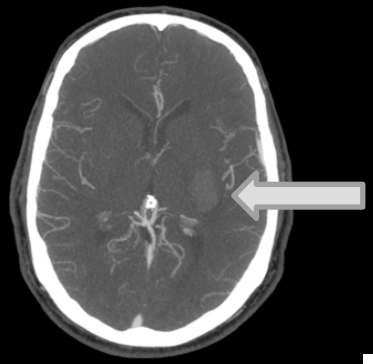
Persistent post-stroke headache is a common issue that is underrepresented in the current literature. It has only recently been recognized this year as a separate entity from acute stroke-attributed headache in the ICHD-3,

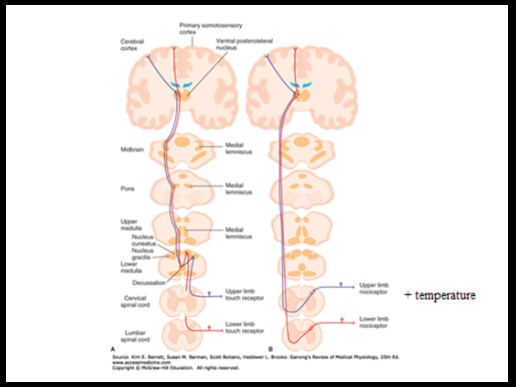
for certain stroke types. Further characterization of its epidemiology, natural history, and options for effective treatment are unmet needs for stroke survivors. Screening, acknowledgment, and therapy may lead to improved rehabilitation outcomes and quality of life.

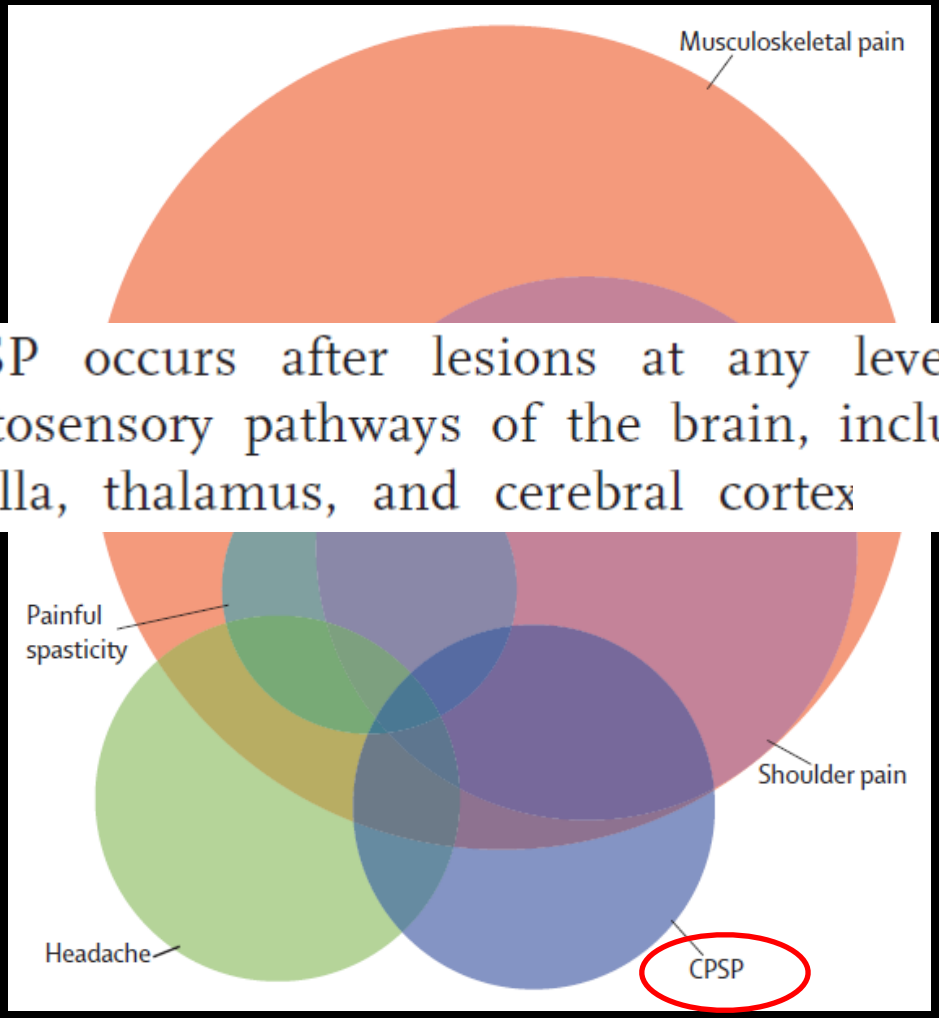
For now, treatment according to semiology since guidelines are lacking and consider contraindications.

Lai et al., 2018

Central post stroke pain=central neuropathic pain







CPSP occurs after lesions at any level of the somatosensory pathways of the brain, including the medulla, thalamus, and cerebral cortex

various combinations of one or several pain types (overlapping areas). The sizes of the circles are approximate to relative frequency (spasticity 7%, headache 10%, CPSP 10%, shoulder pain 20%, musculoskeletal pain 40%). CPSP=central post-stroke pain.

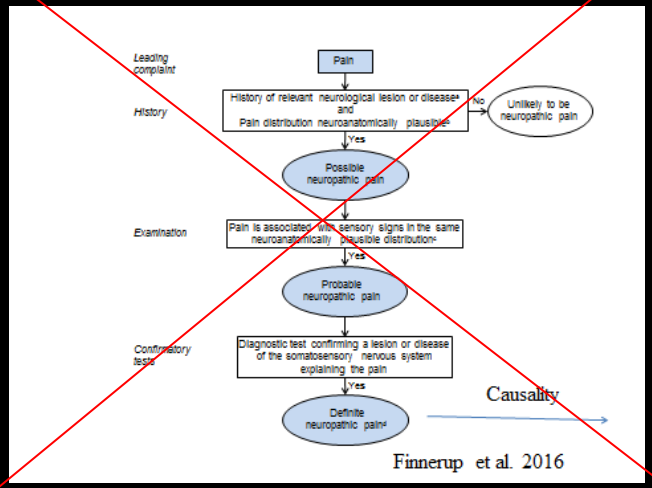
Klit et al., 2009

	Time since stroke	Number of patients	Prevalence of all types of pain	Prevalence of CPSP	Comments
Inpatient rehabilitation multicentre prospective study[21]	Not available	327	Musculoskeletal pain 32·4% (n=106)	4·3% (n=14)	..
Prospective study[22]	12 months	207	..	8% (n=16)	Verified by clinical examination
Stroke register[18]	12 months	253	11% (n=28)	..	..
Acute thalamic infarct verified by CT[8]	Mean 47·5 months (6 months to 9 years)	40	..	8% (n=3) in all patients with thalamic infarct	11% (3 of 27) in patients with sensory dysfunction 17% (3 of 18) in patients with inferolateral infarcts
Questionnaire sent to 1071 elderly individuals (>69 years)[23]	..	72 patients with stroke	..	11% (n=8)	Identified by questionnaire
Stroke unit[17]	3 months	244	55% (n=134)	..	..
Stroke register[16]	16 months	297	All pain 21% (n=62) Stroke-associated pain 8% (n=23)	1% (n=4)	Only patients suspected to have CPSP by interviewers were referred to a neurologist
Outpatient clinic, medullary infarcts: (LMI: n=41; MMI: n=14)[24]	Mean 21 months	55	..	LMI: body 83% (n=34), face 56% (n=23) MMI: body 71% (n=10), face 7% (n=1)	Residual sensory symptoms, not pain
Out-patient rehabilitation clinic[15]	More than 6 months	107	42% (n=45)	12% (n=13)	..
Prophylaxis study of amitriptyline *vs* placebo in patients with acute thalamic stroke[25]	12 months	39	..	18% (pooled; n=7)	Thalamic strokes only Placebo group 21% (4 of 19) Treatment group 17% (3 of 18)
Stroke registry[19]	12 months	140	All pain 49% (n=68) Stroke-associated pain 21% (n=29)	3% (n=4)	..
Patients with LMI identified retrospectively (n=4) and prospectively (n=9), stroke unit[26]	Mean 60 months (2–108 months)	63	..	25% (n=16)	LMI only All patients underwent clinical examination
Severely disabling stroke (Barthel index ≤10), identified by stroke registry and visited at home[20]	12 months	122	Shoulder pain 52% (n=64) Other pain 55% (n=67)	..	..
Postal questionnaire[27]	12 months	119	..	Presumed CPSP 9% (n=11)	CPSP confirmed by clinical examination in 5 of 6 presumed cases (4%)
Inpatient register[28]	24 months	288	15% (n=43)	5% (n=15)	Verified by clinical examination and quantitative sensory tests

..=not applicable. CPSP=central post-stroke pain. LMI=lateral medullary infarct (Wallenberg's syndrome). MMI=medial medullary infarct.

Table 1: **The prevalence of post-stroke pain and CPSP**

Klit et al., 2009



Not available at the time

Prospective study

CHARACTERISTICS OF CENTRAL POST-STROKE PAIN DURING THE FIRST YEAR AFTER STROKE

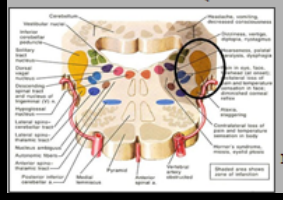
Characteristics	1 month	6 months	12 months *
Survivors able to communicate	207	201	191
No. with CPSP	10 (4.8%)	13 (6.5%)	16 (8.4%)
Pain type			
Burning	1	3	3
Freezing	2	2	3
Aching	2	3	4
Lacerating	6	7	8
Squeezing	2	2	3
Other	1	1	2
Pain duration			
Constant	9	12	14
Daily	1	1	2
Pain severity			
Mild	5	5	6
Moderate	2	5	7
Severe	3	3	3
Pain localization			
Upper extremity	3	4	5
Upper + lower extremity	4	4	5
Hemipain	3	5	6

* One patient who died at 7 months included with scores at 6 months carried forward.

Andersen et al., 1995

Wallenberg syndrome

16/63=25% with CPSP within 6 months (11 within first month)



MacGowan et al. 1997

Prospective-/retrospective study

Table 1 Demographic characteristics of patients

	CVA	SAH	Postoperative infarct	Trauma	MS	AVM	Spinal
Total No of patients	111	19	4	3	4	1	6
Immediate pain	41 (+7 N/K)	2 (+1 N/K)	1	3	—	—	—
Later onset	63	16	3	—	4	9y	6
Age at stroke (y):	n = 111	n = 19					
Mean (SD)	59·2 (9·2)	46·1 (9·6)					
95% CI	57·4–60·9	41·4–50·7					
Median	59	45	—	38·5	58	30	57
Range	40–78	29–62	—	35–42	49–70	—	29–70
Stroke-pain interval (months):	n = 63	n = 16					
Mean (SD)	6·2 (10·0)	4·4 (2·8)					
95% CI	3·7–8·7	2·9–5·9					
Median	3	4					
Range	0·08–72	0·25–12					

Bowsher 1996

Pain always within area of sensory abnormalities

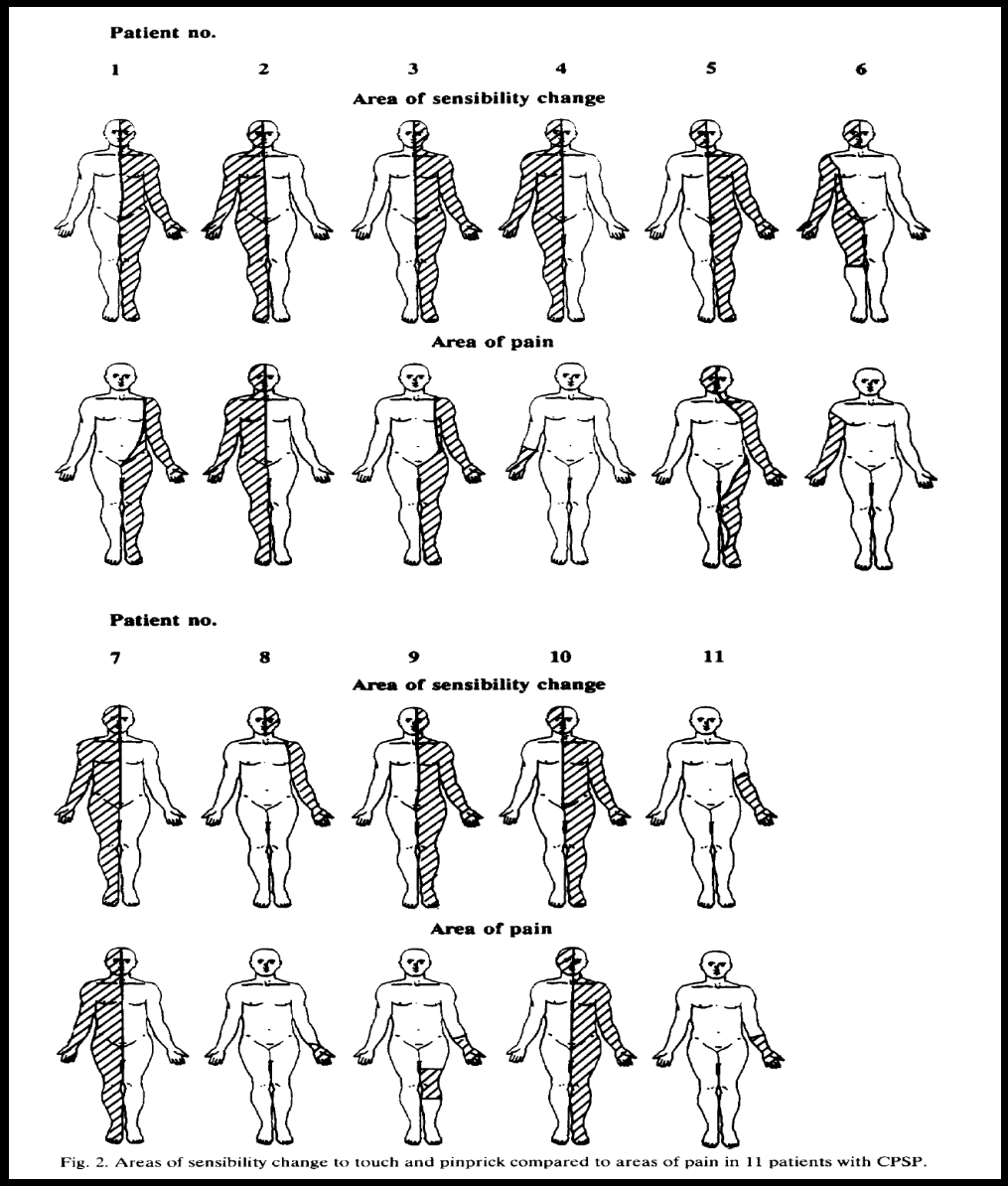
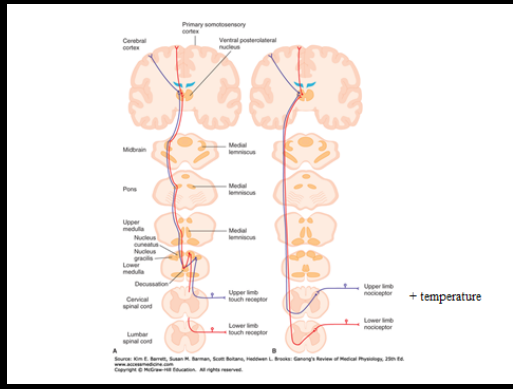


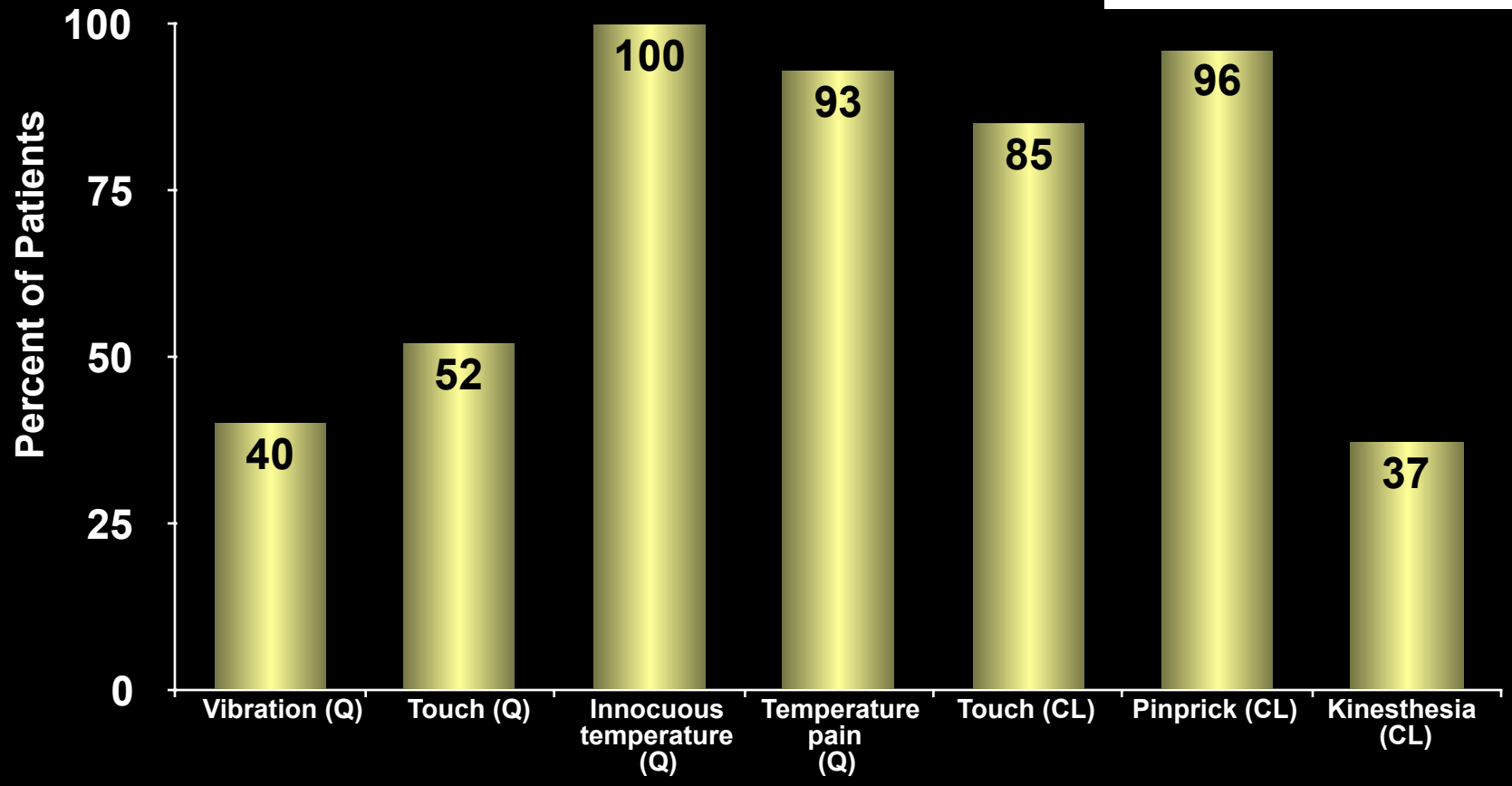
Fig. 2. Areas of sensibility change to touch and pinprick compared to areas of pain in 11 patients with CPSP.

Vestergaard et al., 1995

Somatosensory function in CPSP- any common denominators?

N=27



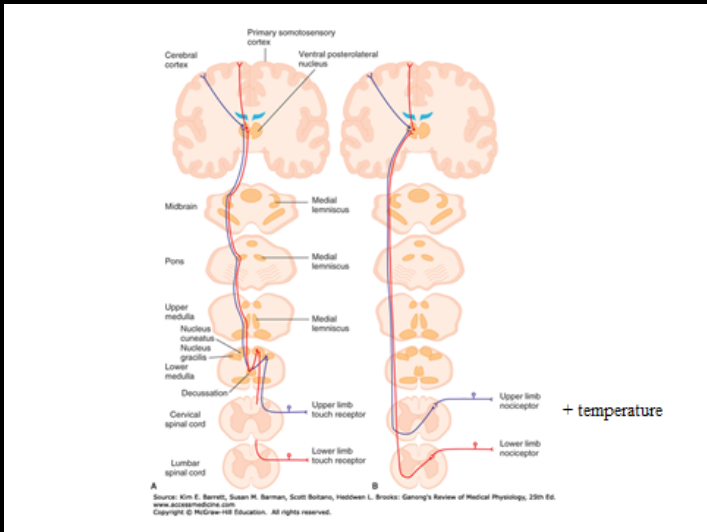


Boivie et al. 1989

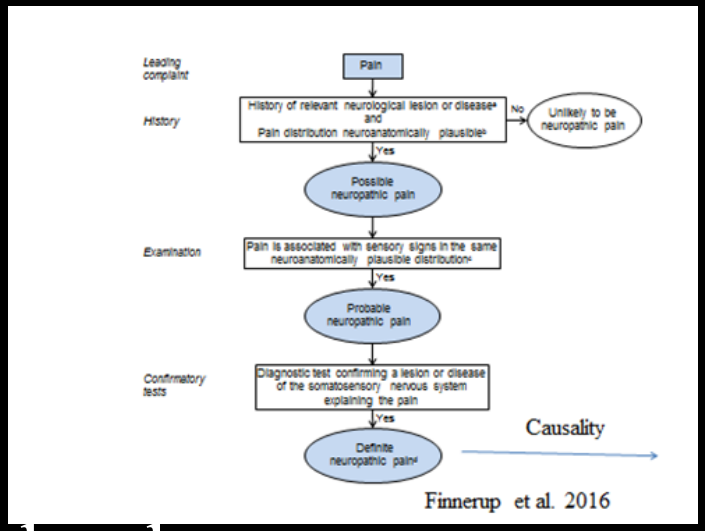
Common denominators in central post stroke pain at sensory examination?

- Spino-(trigemino)-thalamo-cortical pathway affection is a prerequisite, but not the only one
- Nonsensory neurological symptoms and signs may not be present. No correlation between pain and paresis, ataxia or spsticity.

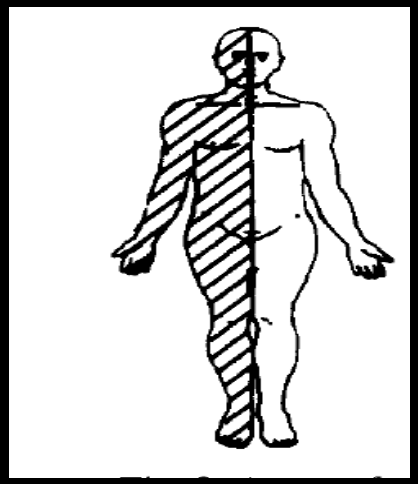
Hansson 2004

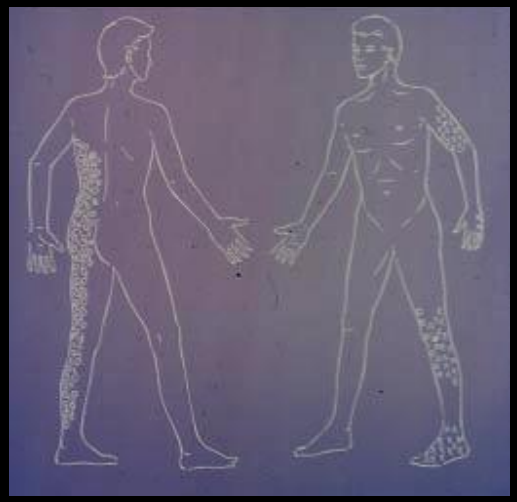


All prerequisites fullfilled but pain still not to be equated with CNeP without further consideration! CAUSALITY?

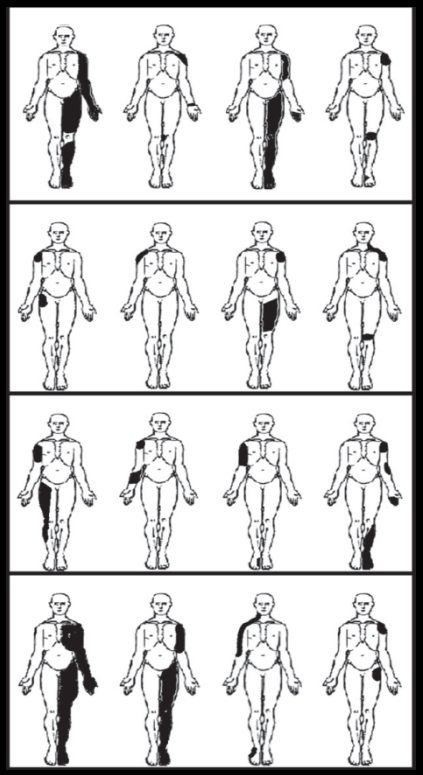


- Post stroke pain:
  - When hemi pain fairly trivial, when patchy--central NeP or m-s pain?





Zeilig et al., 2013



All central neuropathic pains included

	Total daily dose and dose regimen	Recommendations
Strong recommendations for use		
Gapabentin	1200–3600 mg, in three divided doses	First line
Gabapentin extended release or enacarbil	1200–3600 mg, in two divided doses	First line
Pregabalin	300–600 mg, in two divided doses	First line
Serotonin-noradrenaline reuptake inhibitors duloxetine or venlafaxine*	60–120 mg, once a day (duloxetine); 150–225 mg, once a day (venlafaxine extended release)	First line
Tricyclic antidepressants	25–150 mg, once a day or in two divided doses	First line†
Weak recommendations for use		
Capsaicin 8% patches	One to four patches to the painful area for 30-60 min every 3 months	Second line (peripheral neuropathic pain)‡
Lidocaine patches	One to three patches to the region of pain once a day for up to 12 h	Second line (peripheral neuropathic pain)
Tramadol	200–400 mg, in two (tramadol extended release) or three divided doses	Second line
Botulinum toxin A (subcutaneously)	50–200 units to the painful area every 3 months	Third line; specialist use (peripheral neuropathic pain)
Strong opioids	Individual titration	Third line§

GRADE=Grading of Recommendations Assessment, Development, and Evaluation (see appendix for details about the GRADE classification). *Duloxetine is the most studied, and therefore recommended, of the serotonin-noradrenaline reuptake inhibitors. †Tricyclic antidepressants generally have similar efficacy (appendix); tertiary amine tricyclic antidepressants (amitriptyline, imipramine, and clomipramine) are not recommended at doses greater than 75 mg/day in adults aged 65 years and older because of major anticholinergic and sedative side-effects and potential risk of falls;[33] an increased risk of sudden cardiac death has been reported with tricyclic antidepressants at doses greater than 100 mg daily.[34] ‡The long-term safety of repeated applications of high-concentration capsaicin patches in patients has not been clearly established, particularly with respect to degeneration of epidermal nerve fibres, which might be a cause for concern in progressive neuropathy. §Sustained release oxycodone and morphine have been the most studied opioids (maximum doses of 120 mg/day and 240 mg/day, respectively, in clinical trials; appendix); long-term opioid use might be associated with abuse, particularly at high doses, cognitive impairment, and endocrine and immunological changes.[35-37]

Table 2: **Drugs or drug classes with strong or weak recommendations for use based on the GRADE classification**

Order of precedence?

Finnerup et al. 2015

	First-line drugs			Second-line drugs			Third-line drugs	
	Serotonin-noradrenaline reuptake inhibitors duloxetine and venlafaxine	Tricyclic antidepressants	Pregabalin, gabapentin, gabapentin extended release or enacarbil	Tramadol	Capsaicin 8% patches	Lidocaine patches	Strong opioids	Botulinum toxin A
Quality of evidence	High	Moderate	High	Moderate	High	Low	Moderate	Moderate
Balance between desirable and undesirable effects								
Effect size	Moderate	Moderate	Moderate	Moderate	Low	Unknown	Moderate	Moderate
Tolerability and safety*	Moderate	Low-moderate	Moderate-high	Low-moderate	Moderate-high	High	Low-moderate	High
Values and preferences	Low-moderate	Low-moderate	Low-moderate	Low-moderate	High	High	Low-moderate	High
Cost and resource allocation	Low-moderate	Low	Low-moderate	Low	Moderate-high	Moderate-high	Low-moderate	Moderate-high
Strength of recommendation	Strong	Strong	Strong	Weak	Weak	Weak	Weak	Weak
Neuropathic pain conditions	All	All	All	All	Peripheral	Peripheral	All	Peripheral

GRADE=Grading of Recommendations Assessment, Development, and Evaluation (see appendix for details about the GRADE classification). *Common side-effects: antidepressants: somnolence, constipation, dry mouth (particularly with tricyclic antidepressants), and nausea (particularly duloxetine); pregabalin or gabapentin: somnolence, dizziness, and weight gain; opioids (including tramadol): constipation, nausea, vomiting, tiredness, somnolence, dizziness, dry mouth, and itch; lidocaine patches: local irritation; capsaicin patches: local pain, oedema, and erythema; botulinum toxin A: local pain; see the appendix for further information about safety issues.

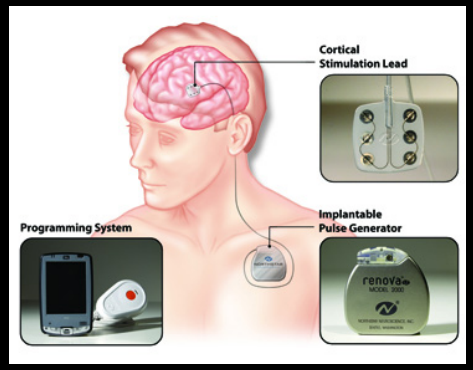
Table 3: Summary of GRADE recommendations

Drug, not specific condition (peripheral or central)

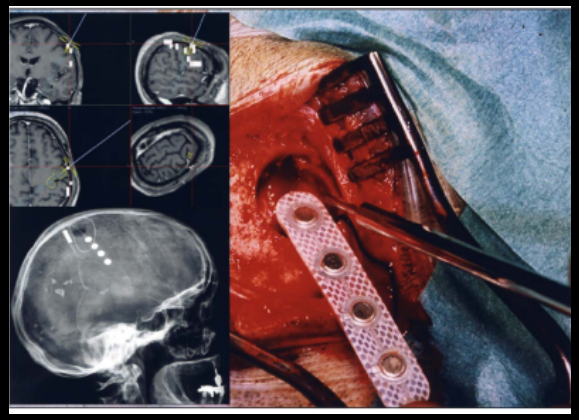
Finnerup et al. 2015

	Comparisons*	Participants†	Active pain relief	Placebo	Number needed to treat (95% CI)	Susceptibility to bias‡
Tricyclic antidepressants	15	948	217/473	85/475	3·6 (3·0–4·4)	1973
Serotonin-noradrenaline reuptake inhibitors	10	2541	676/1559	278/982	6·4 (5·2–8·4)	1826
Pregabalin	25	5940	1359/3530	578/2410	7·7 (6·5–9·4)	2534
Gabapentin§	14	3503	719/2073	291/1430	7·2 (5·9–9·1)	1879
Tramadol	6	741	176/380	96/361	4·7 (3·6–6·7)	982
Strong opioids	7	838	211/426	108/412	4·3 (3·4–5·8)	1326
Capsaicin 8%	6	2073	466/1299	212/774	10·6 (7·4–18·8)	70¶
Botulinum toxin A	4	137	42/70	4/67	1·9 (1·5–2·4)	678

Finnerup et al. 2015



Epidural motor cortex stimulation (Tsubokawa et al., 1991)



Case and observational studies of low to very low quality (Cruccu et al., 2016)

Procedure	Neuropathic pain			
Assessment	Final quality of evidence	Effect size	Tolerability/ safety	Values and preferences
SCS[a]	Low	Low	Moderate	ND
DBS	Very low	Very low	Moderate	ND
MCS	Very low	Low	Moderate	High[b]
rTMS of M1	Low	Low	High	ND
rTMS of DLPFC	Very low	Low	High	ND
tDCS of M1	Low	Low	High	ND
tDCS of DLPFC	Very low	Low	High	ND

Cruccu et al., 2016

The dynamics of post-stroke pain is obvious. Implications for all physicians, nurses, physios and other health care providers:

-Pain after stroke is becoming more prevalent in the aging population.

-Pre-stroke headache and stroke attributed and non-attributed headache should be identified and may change over time. Delayed!

-Delay in start of CPSP is not infrequent. Also difficult with history taking due to cognitive deficits. Behavioral changes may indicate start of CPSP.

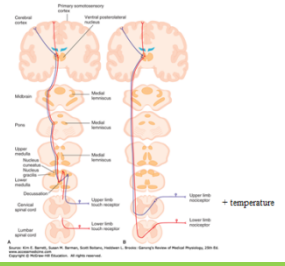
-Involvement of spouses and family members + other relevant personnel. Inform about pain type to patient and relatives.

PAIN

How central is central poststroke pain? The role of afferent input in poststroke neuropathic pain: a prospective, open-label pilot study

2018

Simon Haroutounian[a,b,*], Andria L. Ford[c], Karen Frey[a], Lone Nikolajsen[d,e], Nanna B. Finnerup[d,f], Alicia Neiner[a], Evan D. Kharasch[b,g], Pall Karlsson[d], Michael M. Bottros[a,b]



Rationale and hypothesis: …it is currently unknown whether the sensitization and disinhibition processes after a CNS lesion generate autonomous neuronal activity that is independent from peripheral afferent input. We hypothesized that a stroke-related lesion leads to sensitization of somatosensory CNS neurons in a manner that generates action potentials in response to (previously subthreshold) peripheral sensory input.

See also Cristologo et al., 1991

Table 1

Demographic data and stroke characteristics.

Pt #	Age, sex	Race	BMI	Stroke type	Stroke location	Additional details	Time since stroke	Comorbidities
1	51, F	Black/African heritage	49.2	H	Rt thalamus	Intraventricular extension	6.0 yr	HTN, depression, s/p hysterectomy, dyslipidemia, and DM
2	47, M	Black/African heritage	37.9	H	Rt basal ganglia	Extension into Rt frontal–parietal lobes	6.9 yr	HTN, depression, TIA, CKD, and gout
3	62, M	Caucasian	28.7	H	Lt basal ganglia and thalamus		1.3 yr	HTN, s/p cholecystectomy, and s/p hemorrhoidectomy
4	37, F	Black/African heritage	24.4	H/I	Rt basal ganglia (H) and Rt medial thalamus (I)	Thalamic ischemic stroke occurred 3 months after hemorrhagic stroke	1.7 yr	HTN, depression, DM, and dyslipidemia
5	52, F	Caucasian	28.6	I	Rt thalamus		11 mo	HTN, depression, DM, and dyslipidemia
6	56, M	Black/African heritage	29.0	I	Rt internal capsule		9 mo	HTN and depression
7	60, M	Black/African heritage	28.0	H	Lt basal ganglia	Extension into Lt caudate, thalamus, and lateral ventricle	2.3 yr	Glaucoma, CAD, GERD, CKD, dyslipidemia, and HTN
8	48, F	Caucasian	21	I	Lt basal ganglia, thalamus, and occipital lobe		4.3 yr	Iron deficiency anemia

BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; GERD, gastroesophageal reflux disease; H, hemorrhagic; HTN, hypertension; I, ischemic; IPH, intraparenchymal hemorrhage; Lt, left; NSAID, nonsteroidal anti-inflammatory drug; Rt, right; s/p, status post; TIA, transient ischemic attach.

PAIN

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Table 2
Central poststroke pain characteristics.

Pt #	Pain onset	Pain duration	BPI—pain severity	BPI—pain interference	NPSI total score	Analgesics	Nerve block site
1	Immediate	>5 yr	6.0	5.4	23	Naproxen and acetaminophen (paracetamol)	Left brachial plexus
2	Immediate	>5 yr	6.8	2.4	37	None	Left leg (tibial and peroneal nerves)
3	3-12 months after stroke	6-12 mo	6.0	3.6	49	Tramadol	Right brachial plexus
4	3-12 months after stroke	6-12 mo	5.8	6.6	26	Gabapentin, NSAIDs, and acetaminophen (paracetamol)	Left brachial plexus
5	3-12 months after stroke	6-12 mo	8.5	8.6	58	Gabapentin	Left brachial plexus
6	0-1 month after stroke	6-12 mo	5.0	5.6	26	None	Left leg (tibial and peroneal nerves)
7	0-1 month after stroke	2-5 yr	7.5	6	60	Gabapentin	Right brachial plexus
8	Immediate	2-5 yr	4.8	2.7	34	Duloxetine	Right elbow (ulnar, radial, and median nerves)

BPI, Brief Pain Inventory; NPSI, Neuropathic Pain Symptom Inventory; NSAIDs, nonsteroidal anti-inflammatory drugs.

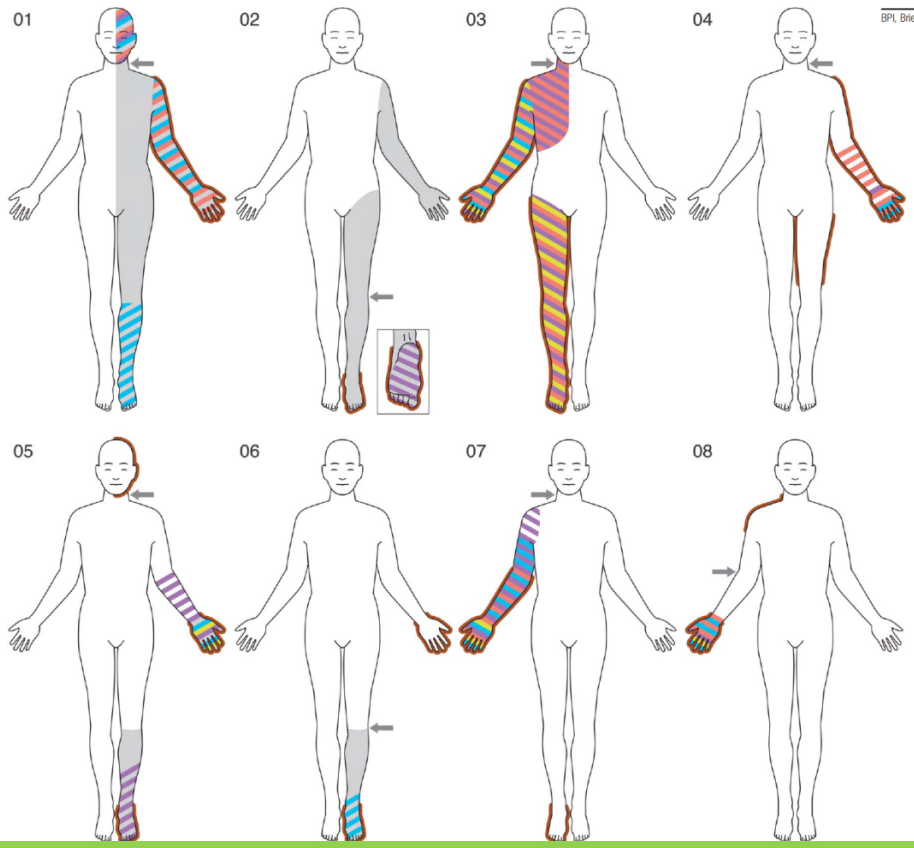

Figure 1. Distribution of spontaneous pain and sensory disturbances. Gray shading= sensory loss; diagonal lines = hypersensitivity to heat (red), cold (blue), pinprick (purple), and brush (yellow**). The circumferential dark red lines indicate area(s) of spontaneous ongoing pain. Arrows indicate the anatomical location where peripheral nerve block was performed**. No placebo control.

PAIN

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Results:

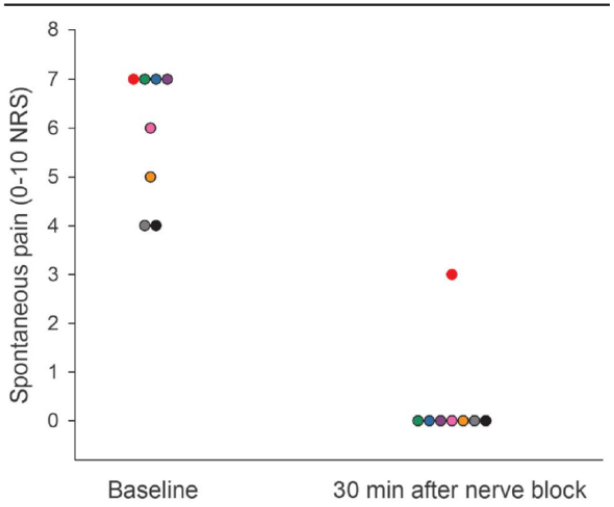

Figure 2. Primary outcome of change in spontaneous pain. Intensity of ongoing pain at baseline (before the block) and 30 minutes after the block (primary outcome). Each subject is coded by a different color. NRS, numerical rating scale.

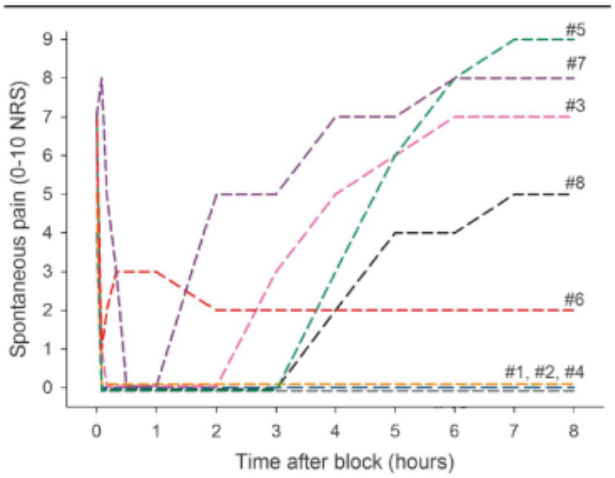

Figure 3. Individual pain score changes after the nerve block. After the peripheral nerve blockade, pain intensity returned to baseline within 4 to 7 hours in 4 patients, consistent with the duration of lidocaine action. In 3 patients, pain scores remained zero for 8 hours after the nerve block, in 1 patient (#4, baseline NRS = 7), pain intensity remained at NRS = 2. NRS, numerical rating scale.

Table 3

Intensity scores for thermal and mechanical sensation in the painful extremity.

Sensory modality	Baseline	30 minutes after the block	*P*
Cold	7 (4.5-7.8)*	0 (0.0-1.5)*	0.008
Heat	5.9 (±1.4)	0.5 (±1.1)	<0.0001
Brush	4.5 (±1.9)	1.0 (±1.4)	0.004
Pinprick	5.0 (±2.1)	1.1 (±2.2)	0.003

Scores were assessed on a scale from 0 to 10, where 5 is "normal sensation" tested against a contralateral, nonpainful area; lower scores represent hyposensitivity (0 = no sensation), and higher scores represent hypersensitivity (10 = most intense/painful sensation).

* Data were not normally distributed (Shapiro–Wilk test), therefore analyzed by the Wilcoxon signed rank test, and presented as median (interquartile range).

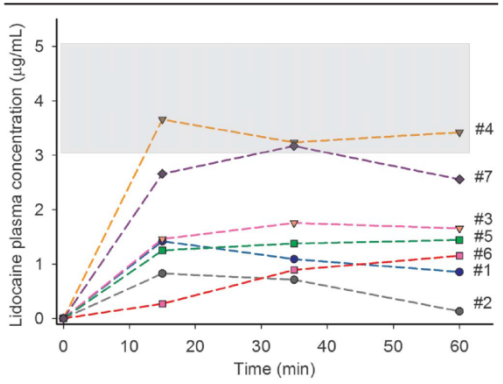

Figure 4. Plasma lidocaine concentrations after the nerve block. Individual plasma concentrations of lidocaine measured at baseline and 15, 35, and 60 minutes after the nerve block. Because of technical reasons, lidocaine concentrations in 1 patient (#8) were not analyzed. The shaded area represents the concentration range (3-5 µg/mL) associated with potential systemic analgesic effect of lidocaine.

PAIN

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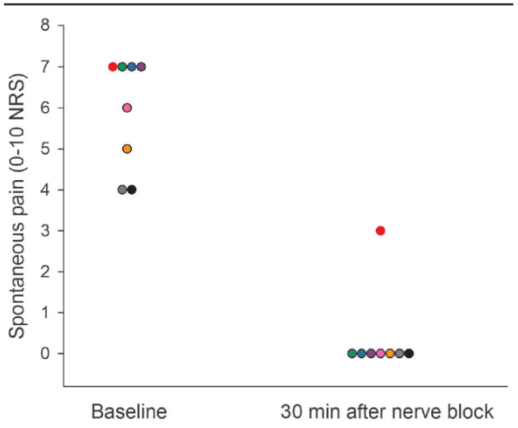

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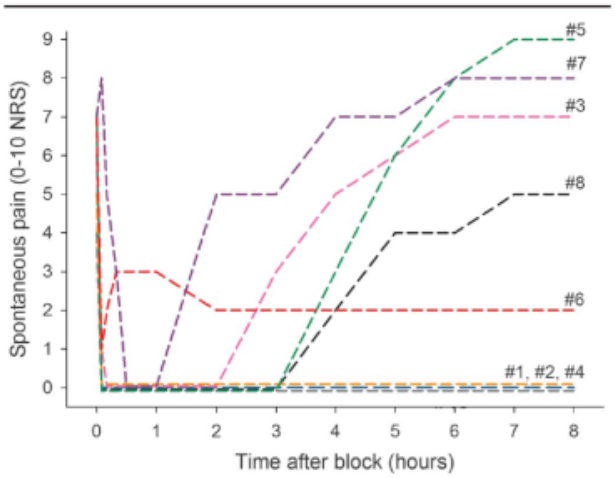

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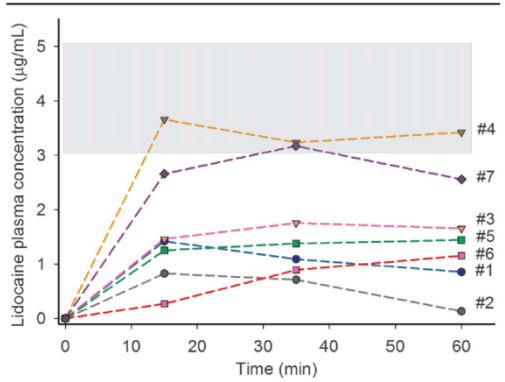

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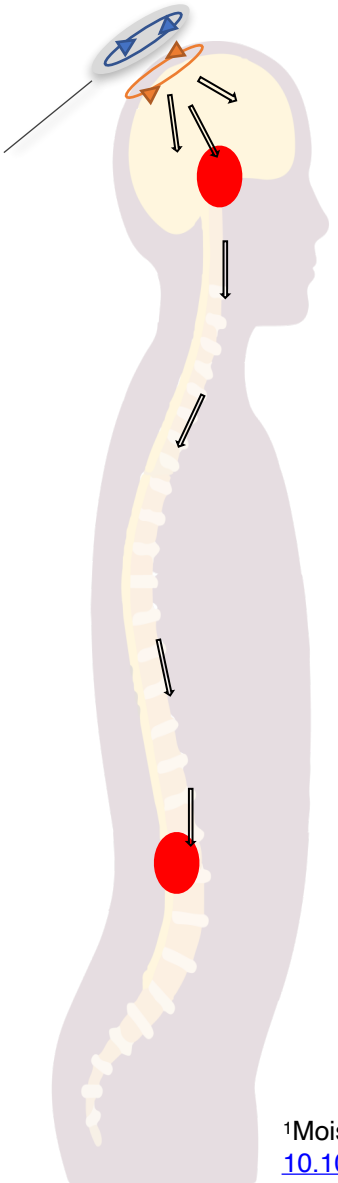
? Have a confused weekend!

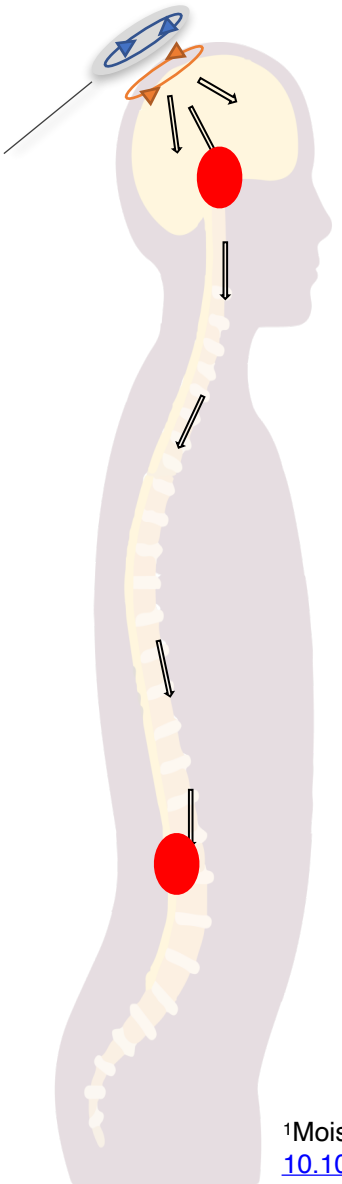
HNEP studie

- Multisenterstudie i samarbeid med:
  - Centre d'Evaluation et de Traitement de la Douleur, Hôpital Ambroise Paré, Paris
  - Service d'exploration fonctionnelle, Hôpital Henri Mondor, Paris
- Formål
  - Sammenligne effekten av repetetiv transkraniell magnetisk stimulering (rTMS) med to ulike magnetspoler for å behandle sentrale nevropatiske smerter etter ryggmargsskade eller slag.



- TMS bruker svingninger i magnetfelt for å produsere elektrisk strøm i hjernebarken
- Ved repetetiv stimulering aktiverer TMS områder i hjernen involvert i smerteopplevelse og nedadgående smertebaner fra hjernestammen til ryggmargen
- rTMS påvirker også opioid-, GABA- og dopamin- medierende effekter i nervesystemet, som er involvert i smerteprosessen[1]

[1]Moisset et al. (2016) https://doi.org/10.1002/ejp.811



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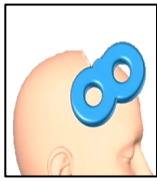
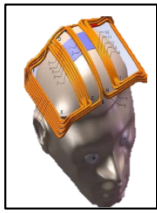


Figur-8-spole

- Stimulerer et lite og overfladisk område av hjernebarken
- Høyfrekvent rTMS til motoriske områder i hjernebarken gir kun moderate effekter[2]



H-spole

- Stimulerer dypere og flere områder av hjernen
- Smertestillende effekt i en RCT pilotstudie hos pasienter med smertefull diabetisk polynevropati[3]
- H-spole gir bedre effekt enn figur-8-spolen ved perifere nevropatiske smerter i lavere ekstremiteter når man stimulerer det området i hjernebarken ansvarlig for disse lemmene [4]

[1]Moisset et al. (2016) https://doi.org/10.1002/ejp.811

[3]Onesti et al. (2013) https://doi.org/10.1002/j.1532-2149.2013.00320.x

[4] Shimizu et al (2017) https://doi.org/10.3171/2016.9.JNS16815

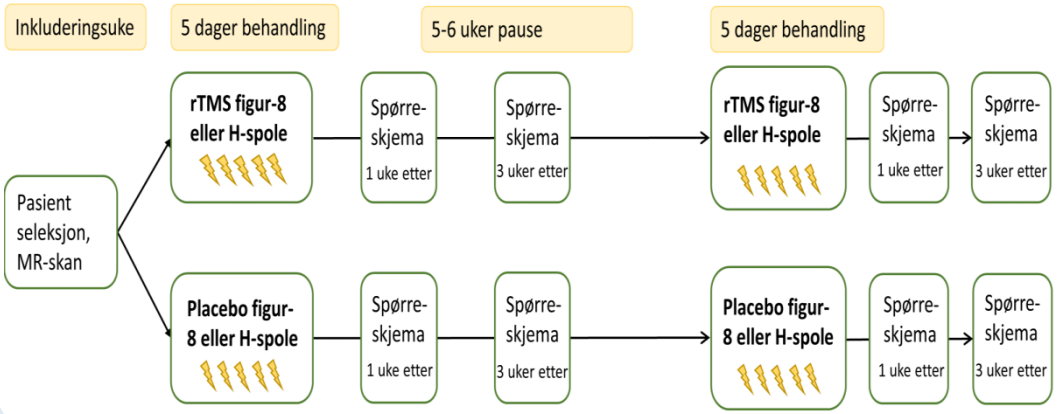
SPØRSMÅL

- Vil rTMS redusere nevropatisk smerte til forskjell fra en placebo (sham) gruppe?
- Hvilken rTMS behandling vil gi bedre effekt, H-spole eller figur-8 spole?

H-spole

Figur-8-spole

PROTOKOLL



INKLUSJONSKRITERIER

- Sentral nevropatisk smerte (ryggmargsskade, slag) i minst 6 måneder
- Smerte tilstede minst 4 dager i uken
- Alder: 18-80 år