Appendix e-2

Reaching consensus and Search strategy

Initially, two authors (G.C. and T.N.) identified the problem and identified participants with expertise within TN and/or neuropathic pain classification. These participants were asked to further identify possible experts. Our aim was not to have the view of neurologists, only, but also include neurosurgeons, neurophysiologists, and experts on oral-facial pain. All experts were invited to participate via e-mail. The first part of the process consisted of a thorough review of the literature looking first for clinical guidelines, then meta-analyses, and finally to original research reports in at least 10 patients. The Medline database was searched and additional studies were sought from the reference list of retrieved papers. Eligibility was initially determined by reading the title and abstracts identified in each search. Full-length articles of potentially eligible studies was obtained and assessed. One author provided a summary of the results and all authors were provided with all the documentation. The results were discussed among all authors via email. A dedicated meeting was held in Nice in 2015 in the occasion of NeupSIG world congress, where we were able to come to an agreement on the diagnostic flow-chart and decided to keep in it the three levels of diagnostic certainty for trigeminal neuralgia consistent with the grading system for neuropathic pain (Treede et al. Neurology 2008) and its updated version (Finnerup et al. Pain, in press). After final discussions a first draft was the result of interaction between five authors (G.C., T.N., N.B.F., J.S., and R-D.T.). This primary draft was circulated to and revised by all authors, until the final manuscript was agreed on by consensus of the authors.

In particular we decided that the following issues needed a dedicated literature search:

Involvement of ophthalmic division as a sign of secondary TN.

This issue was already searched for in the Euro-American guidelines: a meta-analysis brought to the conclusion that involvement of the first division of the trigeminal nerve is probably not associated with an increased risk of secondary TN (refs 4,5 of main text).

Involvement of the tongue as a sign of secondary TN.

We used the search string: trigeminal neuralgia[title] AND tongue[title/abstract] and found 10 titles, none of them relevant to the question.

Bilateral classical or idiopathic TN.

This issue was already searched for in the Euro-American guidelines: a meta-analysis did not reveal any report of truly bilateral TN in 234 patients with classical TN (refs 4,5 of main text).

Bilateral TN associated with multiple sclerosis.

We used the search string: multiple sclerosis [title] AND trigeminal neuralgia[word text] AND bilateral [word text] and found 11 titles + found 3 more because known to the panel or found in the references. Of these 14 titles, 9 were not relevant or reported occasional patients. The five selected studies described a total of 252 patients with TN associated with multiple sclerosis; in 24 of these TN was “bilateral” (refs 16-20 of main text).

Trigger in classical TN.

Using the string "no trigger" OR "without trigger" OR "absence of trigger" OR "spontaneous alone” OR "spontaneous pain alone" OR "spontaneous only" OR "spontaneous pain only", ALL FIELDS, we found no references.

Using the string trigeminal neuralgia[title] AND trigger[title/abstract], we found 65 titles. Of these, only 4 studies faced directly the problem and were based on a cohort of more than 10 patients. Out of a total of 410 patients with classical TN, 404 did report trigger zones or manoeuvres (refs 11,21-23 of main text)

Frequency of secondary TN

This issue was already searched for in the Euro-American guidelines: a meta-analysis brought to the conclusion that out of 243 TN patients, 35 had multiple sclerosis or a cerebellopontine angle tumour, which caused TN (refs 4,5 of main text).

Diagnostic accuracy of neurophysiological tests.

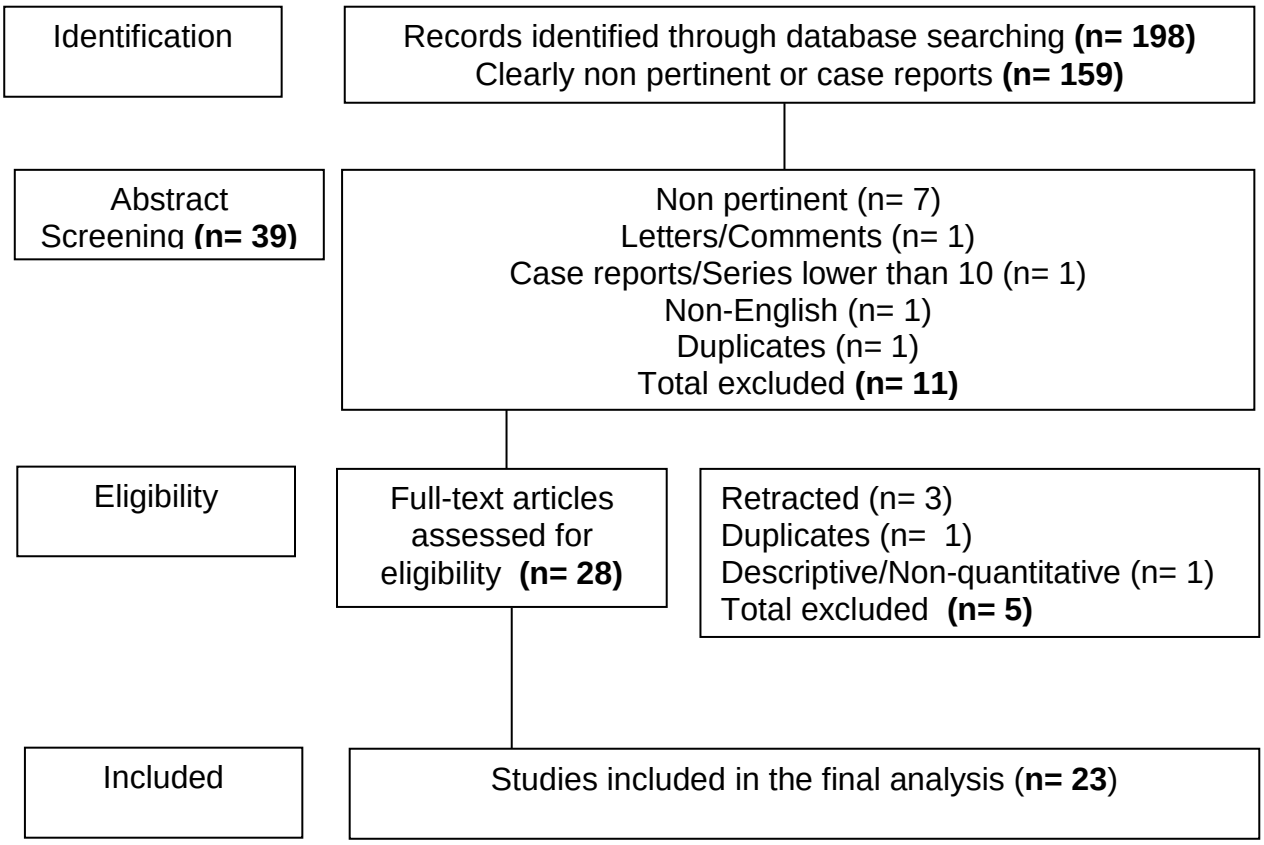
This issue was already searched for in the Euro-American guidelines: one meta-analysis brought to the conclusion that trigeminal reflex testing disclosed abnormalities in 54/62 of patients with secondary TN and 14/244 patients with classical TN, thus yielding 87% sensitivity and 94% specificity. Another meta-analysis assessed the diagnostic accuracy of trigeminal evoked potentials, which were found abnormal in 48/57 patients with secondary TN and 55/152 patients with classical TN, yielding 84% sensitivity and 64% specificity (refs 4,5 of main text).

Association between neurovascular compression and TN as assessed by MRI.

Using the string: trigeminal neuralgia AND (MRI OR magnetic resonance imaging)

Filters: Humans, Title/Abstract, From 2008/01/01 to 2014/12/31

We found 198 references (Prisma Chart):



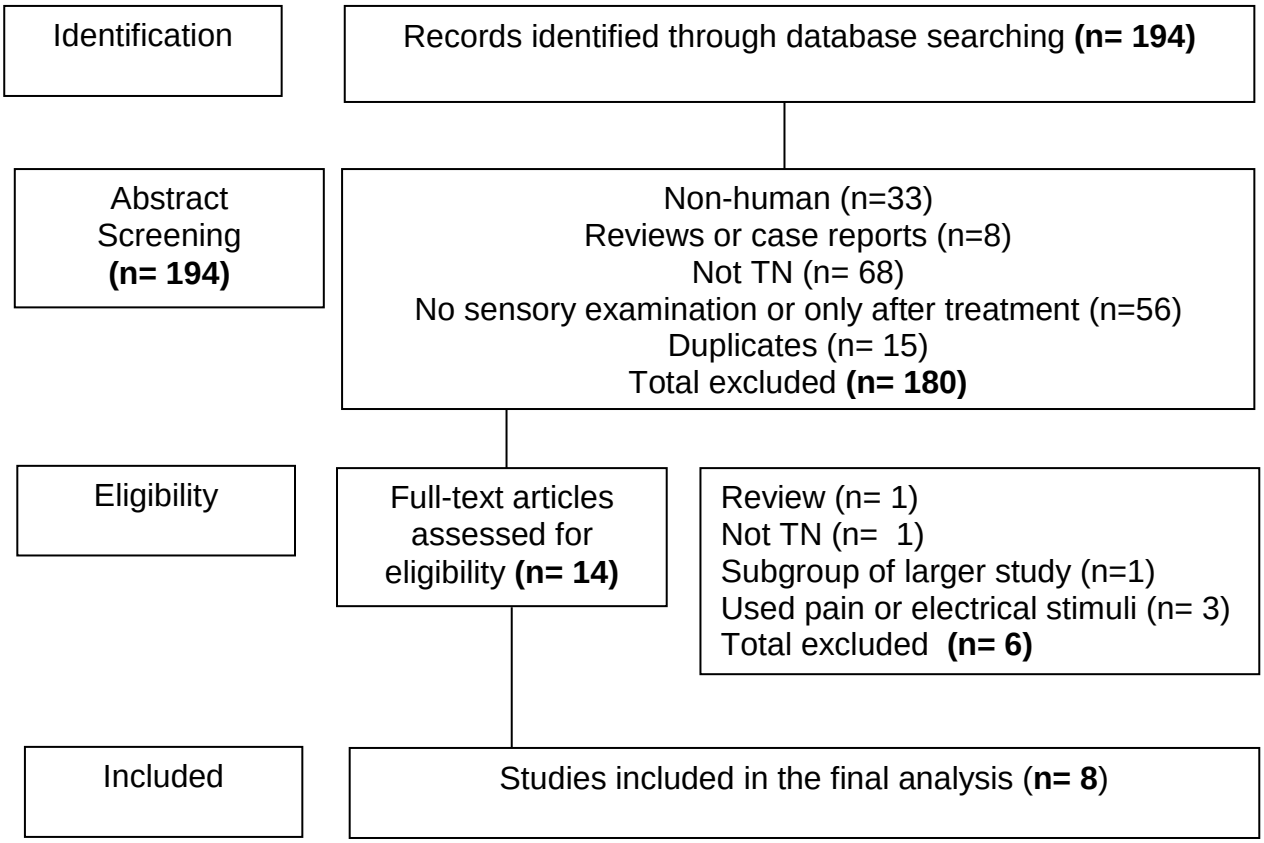
Among the eligible studies there was a recent meta-analysis (ref. 35 of main text) of 9 high-quality blinded and controlled studies, reported a total of 471/531 contacts on the symptomatic side (89%) and 244/681 on the contralateral side (36%). In our list we found 12 high-quality studies, which reported a total of 665/772 contacts on the symptomatic side and 321/900 contacts on the contralateral side, thus yielding 86% sensitivity and 64% specificity. Looking for morphological changes of the trigeminal nerve root (dislocation, distortion, flattening or atrophy, contact at root entry zone) we calculated a total of 280/466 with morphological changes and 94/897 without, which yielded 60% sensitivity and 89% specificity.

Sensory abnormalities in quantitative sensory testing (QST)

Using the string: "Trigeminal neuralgia" AND (QST OR "quantitative sensory testing"), or “trigeminal neuralgia thermal” or “trigeminal neuralgia sensory thresholds”.

Up to 2014/12/31

We found 193 references (Prisma Chart):



We found 8 studies that reported sensory changes in classical or idiopathic TN. The studies included in total 281 patients with TN, 105 controls and 139 patients with other pain conditions. Five studies included a control group or compared the results to a normal material while two studies compared to contralateral side only and comparison in one study was unclear. Methods and outcomes were too variable to perform a meta-analysis. Two studies provided data on percentage with abnormal sensory findings on QST; one found abnormal sensory function in 87% of patients (ref to Maier 2010) while the other found abnormal sensory function in 58% (ref to Nurmikko 1991). Studies reporting differences in group (mean) results found both increased thermal and mechanical detection thresholds.