PAIN® 155 (2014) 2699–2706

www.elsevier.com/locate/pain

Early evoked pain or dysesthesia is a predictor of central poststroke pain

Henriette Klit [a,b,*], Anne P. Hansen [a], Ninna S. Marcussen [a], Nanna B. Finnerup [a], Troels S. Jensen [a,b]

[a] Danish Pain Research Center, Aarhus University, Aarhus, Denmark
[b] Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 29 June 2014
Received in revised form 26 September 2014
Accepted 29 September 2014

Keywords:
Central neuropathic pain
Central poststroke pain
Pain
Predictors
Stroke

ABSTRACT

Central poststroke pain (CPSP) is a central neuropathic pain condition caused by a cerebrovascular lesion affecting the central somatosensory nervous system. Once developed, CPSP is difficult to treat, so there is an interest in identifying stroke patients at risk for the development of CPSP. This study examined if sensory abnormalities, including evoked dysesthesia, allodynia, or hyperalgesia to static and dynamic touch, cold, and pinprick, at stroke onset are a predictor for the development of CPSP. Consecutive stroke patients were recruited from a large prospective study of poststroke pain in Aarhus, Denmark, between 2007 and 2008. Patients underwent a structured pain interview and a standardized sensory examination within 4 days of admission, and a structured telephone interview was conducted after 3 and 6 months. Patients who developed poststroke pain in the affected side without any other plausible cause were classified as having possible CPSP. A total of 275 stroke patients completed the study, and 29 patients (10.5%) were classified as having possible CPSP. The diagnosis was confirmed by a clinical examination in 15 of 17 patients, corresponding to a prevalence of 8.3%. The presence of allodynia, hyperalgesia, or dysesthesia in response to the sensory examination at stroke onset increased the odds for CPSP at 6 months by 4.6 (odds ratio; 95% confidence interval 1.5–13.9). The combination of reduced or absent sensation to pinprick or cold and early evoked pain or dysesthesia at onset increased odds by 8.0 (odds ratio; 95% confidence interval 2.6–24.8). In conclusion, early evoked pain or dysesthesia is a predictor for CPSP.

1. Introduction

Central poststroke pain (CPSP) is a central neuropathic pain condition caused by a vascular lesion of the central somatosensory nervous system [16]. It is characterized by pain and sensory abnormalities in the body parts that correspond to the injured brain area. The incidence of this devastating condition, which is associated with both reduced quality of life and increased mortality [7,27], is estimated to be 7% to 8% in stroke survivors [1,19]. The condition is often refractory to treatment, and it is thus important to identify patients who are at risk for the development of CPSP in order to follow these patients more carefully, inform them about central pain, initiate treatment, and conduct prophylactic treatment studies in the future.

The underlying mechanisms of CPSP are not known, but abnormal spinothalamocortical tract function [23,34], loss of inhibition [6,9,11,12,14], central sensitization [37], and neuroplastic changes [24,28,29] are all mechanisms that have been implicated in this and other central neuropathic pain conditions. Central sensitization is defined as an increased responsiveness of nociceptive neurons in the central nervous system (CNS) to their normal or subthreshold afferent input [1].

Neuropathic pain is characterized by negative and/or positive symptoms and signs. It may be spontaneous (ongoing or intermittent) or evoked, and it may be associated with nonpainful dysesthesia or paresthesia [5,34]. The negative signs in CPSP include loss or reduction of thermal and pinprick sensibility, while positive symptoms and signs are pain or unpleasantness evoked by touch, pressure, or thermal stimuli. This dual combination of loss and hypersensitivity in the affected area is usually explained by loss of input to a population of CNS neurons participating in the processing of somatosensory information, and at the same time hyperexcitability in the same or other neurons within the CNS [14,19].

Our previous studies have shown that sensory hypersensitivity in the affected body parts may occur already at onset of stroke [1,19], but it is unclear if this sensory hypersensitivity presenting as hyperalgesia, dysesthesia, or allodynia is a risk factor for the

* Corresponding author at: Danish Pain Research Center, Aarhus University Hospital, Norrebrogade 44, Building 1A, DK-8000 Aarhus C, Denmark. Tel.: +45 7846 3287; fax: +45 7846 3269.
E-mail address: henriette.klit@clin.au.dk (H. Klit).

http://dx.doi.org/10.1016/j.pain.2014.09.037
0304-3959/

subsequent development of pain. In 2 recent studies, early sensory hypersensitivity was found to predict later onset of central neuropathic pain (below-level pain) in patients with spinal cord injury [10,38]. In this prospective study, we aimed to determine if stroke patients with early evoked pain or dysesthesia, defined as findings of allodynia, hyperalgesia, or dysesthesia in response to the sensory examination at stroke onset, have an increased risk of developing CPSP.

2. Methods

2.1. Patient recruitment

We included stroke patients admitted consecutively to the Stroke Unit of the Department of Neurology, Aarhus University Hospital, Aarhus, Denmark, between February and September 2007 and between February and July 2008 (Fig. 1). Inclusion criteria were age of 18 years or above, informed consent, and a diagnosis of stroke according to the World Health Organization criteria (ICD-10 codes: I61, I63, I64.9, I67.6, and I67.7). Exclusion criteria were a diagnosis of trasient ischemic attack (TIA) (G45.9) or subarachnoid hemorrhage (I60.9), inability to communicate, severe dementia, or pronounced somnolence. Results on pain development are reported elsewhere [13].

All included patients underwent a structured interview and a standardized bedside sensory examination within the first 4 days of admission (initial examination), including sensory testing for dysesthesia, allodynia, and hyperalgesia. Dysesthesia is defined as an unpleasant abnormal sensation, whether spontaneous or evoked; allodynia as pain due to a stimulus that does not normally provoke pain; and hyperalgesia as increased pain from a stimulus that normally provokes pain [26]. To determine the presence of these phenomena, we used static and dynamic touch, cold, and pinprick stimulation (in the following called evoked pain or dysesthesia) [13]. The interview included questions about pain conditions before the stroke and the presence of spontaneous and evoked pain or dysesthesia at or after stroke onset. Medical records from the hospital admission and results of computed tomography (CT) and/or magnetic resonance imaging (MRI) scans were obtained. All initial examinations were done by 1 of 2 investigators (APH or NSM).

A structured follow-up telephone interview was conducted 3 and 6 months after stroke onset. The interview included questions

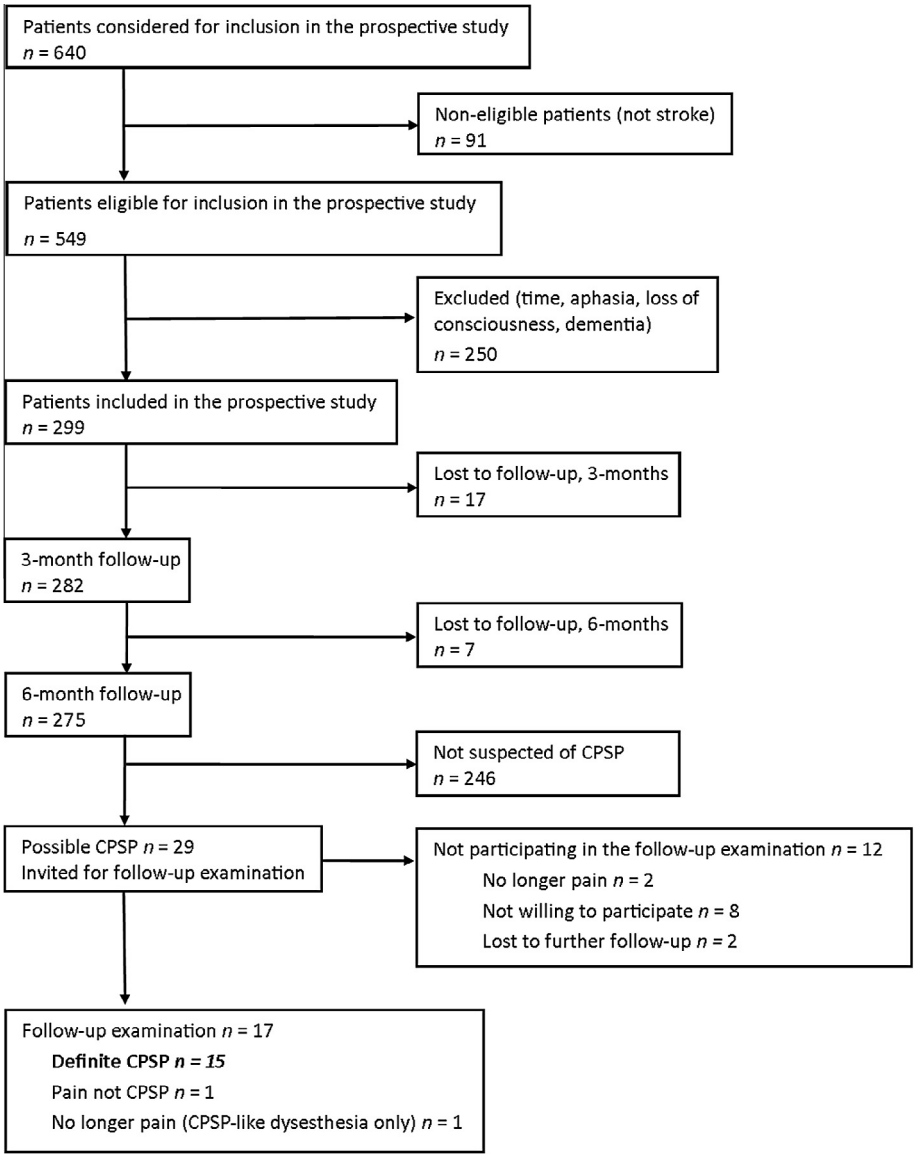

Fig. 1. Flow chart of study.