Trigeminal Autonomic Cephalalgias (TACs) – SUNCT/SUNA

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Introduction

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are rare headache syndromes which make up the trigeminal autonomic cephalalgias (TACs), along with cluster headache and paroxysmal hemicrania. All of the TACs are characterized by attacks of severe or excruciating unilateral facial and head pain associated with ipsilateral cranial autonomic symptoms such as conjunctival injection, lacrimation, nasal blockage, rhinorrhoea, ptosis, and eyelid edema. SUNCT and SUNA are the rarest of the TACs, and are characterized by the shortest duration of attacks. In SUNCT, by definition, conjunctival injection and lacrimation are present. SUNCT forms the majority subset of SUNA, where there are any or all of the cranial autonomic symptoms. In SUNA, there may be conjunctival injection, lacrimation, neither of these, but not both.

Clinical Characteristics

The attacks of SUNCT/SUNA are short-lived, lasting from 2 to 240 s per attack. Attacks can occur as single stabs, groups of stabs, or with a saw-tooth pattern of a painful attack with stabs superimposed (Figure 1). The groups of stabs or the saw-tooth attacks may last considerably longer than 240 s (reported up to 3600 s), and therefore some cases may be incorrectly diagnosed as one of the longer-acting TACs. The International Headache Society Classification Criteria for SUNCT are listed below. There should be at least 20 attacks fulfilling criteria 2–4:

1. Attacks of unilateral orbital, supraorbital, or temporal stabbing or pulsating pain lasting 5–240 s.
2. Pain is accompanied by ipsilateral conjunctival injection and lacrimation.
3. Attacks occur with a frequency from 3 to 200 per day.
4. Not attributed to another disorder.

As with the other TACs, SUNCT can be either episodic (in bouts of a few weeks or months at a time with remission periods of several months) or chronic (with attacks for over a year without a break of more than a month). SUNA is usually chronic. This is in contrast to cluster headache, where the majority of cases are of the episodic form.

The pain is usually around the eye and in the retroorbital region, but can be anywhere in the face or on the ipsilateral side of the head. Cranial autonomic symptoms are almost exclusively ipsilateral to the pain. Attacks can be spontaneous, or triggered by touching the side of the face, chewing, talking, cold wind on the face, and brushing the teeth, amongst others. Trigger factors are more readily recognized in SUNCT (79%) than in SUNA (33%). Attacks can also wake the patient at night. There is typically no refractory period between attacks; one attack can be triggered immediately after another. Often the patient is agitated with pain, as with other TACs, and this can be a useful distinguishing feature from trigeminal neuralgia.

Some patients have a constant background pain with attacks superimposed. These patients often have a personal or family history of migraine and/or medication overuse. Migrainous...
symptoms such as nausea, photophobia, and phonophobia can also be present, although in a minority of patients. The photophobia and phonophobia in migraine is usually bilateral, yet where it occurs in TACs it is often ipsilateral to the side of the pain.

**Epidemiology**

SUNCT/SUNA are rare syndromes, with an uncertain incidence and prevalence. They can affect all ages, with reports from 5 to 88 years old, but typically the onset is at age 35–65 years. SUNCT has a slight male predominance (1.4:1), more so possibly in SUNA (2:1), although the data sets are so small that it is difficult to extrapolate.

**Differential Diagnosis**

The differential diagnosis for SUNCT/SUNA and some clinical similarities and distinguishing features are outlined in Table 1.

**Secondary/Symptomatic SUNCT/SUNA**

Most patients have idiopathic or primary SUNCT/SUNA, that is, without an underlying structural cause. However, a small but significant proportion of patients have an associated abnormality, usually in the posterior fossa or the brainstem. Some of these are listed in Table 2. There is also a group of patients with pituitary adenomas, either micro- or macroadenomas, with headaches secondary to these. The headache may take any form, but SUNCT/SUNA are disproportionately represented within this cohort of patients. Headache syndromes may precede the discovery of the tumor by up to 10 years. Treatment of the pituitary lesions, either with dopamine agonists or hypophysectomy, may have either a beneficial or a detrimental effect on the attacks of SUNCT, or may indeed precipitate an initial bout of SUNCT in patients previously unknown to have this condition. Other causes are listed in Table 2.

**Posttraumatic SUNCT/SUNA**

As with other headache syndromes, posttraumatic SUNCT and SUNA have been reported to occur after a traumatic head injury. The purported mechanism in posttraumatic migraine is axonal injury or a shearing effect to the brainstem even after mild or moderate injury, which would cause a physiological shift in the brainstem, leading to chronic migraine. It is possible that a similar posttraumatic physiological abnormality in the brainstem or hypothalamus, or indeed activation of a preexisting disposition to such abnormality, may lead to the development of SUNCT or SUNA.

**Pathophysiology**

**Hypothalamic Hypothesis**

Functional imaging work in PET and functional magnetic resonance imaging (MRI) have shown activation in the region of the posterior hypothalamus in patients with primary SUNCT and SUNA, as in the other TACs. Given that SUNCT shares clinical features of prominent cranial autonomic symptoms with other TACs, a hypothalamic–trigeminal–autonomic pathway is suspected. Moreover, the agitation associated with the attacks of all of the TAC types may represent activation of the region of the posterior hypothalamus. Deep brain

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Similarities to SUNCT/SUNA</th>
<th>Clinical distinguishing features for SUNCT/SUNA</th>
<th>Distinguishing features for differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal hemicrania (PH)</td>
<td>Short-lasting attacks with autonomic symptoms</td>
<td>Attacks can be triggered by touching the face. Very short and large number of attacks (groups of stabs or saw-tooth attacks giving the impression of longer attacks)</td>
<td>PH attacks typically 2–30 min, up to 40 attacks/day PH responds to indomethacin</td>
</tr>
<tr>
<td>Cluster headache (CH)</td>
<td>May be confused with long groups of SUNCT/SUNA stabs</td>
<td>CH attacks typically 15–180 min, up to 8 attacks/day CH responds to inhaled oxygen and subcutaneous sumatriptan</td>
<td></td>
</tr>
<tr>
<td>Trigeminal neuralgia (TN)</td>
<td>Short-lasting attacks, triggered by touching face, may have associated autonomic symptoms</td>
<td>Autonomic symptoms much more prominent Agitation with attacks No refractory period between attacks</td>
<td></td>
</tr>
<tr>
<td>Hemicrania continua (HC)</td>
<td>In cases where the background pain is prominent</td>
<td>A clear history of short-lasting stabs or groups of stabs; prominent autonomic features</td>
<td>HC responds to indomethacin</td>
</tr>
</tbody>
</table>

Abbreviations: SUNA, short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms; SUNCT, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.
hypothalamic stimulation has been effective in the treatment for some TAC patients, including cluster headache and SUNCT.

**Trigeminal Nerve Hypothesis**

Although data are limited, several studies have reported the presence on brain MRI of a vascular loop contacting or compressing the trigeminal nerve ipsilateral to the pain of SUNCT/SUNA. It is possible, therefore, that the peripheral mechanisms may also play a key role in the pathophysiology of SUNCT. Furthermore, some patients with SUNCT/SUNA may benefit from trigeminal microvascular decompression, and patients may respond to medical treatment such as carbamazepine or gabapentin, which are typically used in trigeminal neuralgia.

**Making a Diagnosis of SUNCT/SUNA**

**History**

The clinical history is paramount in making a diagnosis of SUNCT/SUNA. In particular, the length and frequency of attacks (as in Figure 1), type of pain (severe, often stabbing in nature, may have other characteristics), periodicity and chronicity, the presence or absence of cranial autonomic symptoms, agitation, triggering, and lack of refractory period between attacks should be elicited from the history. A personal or family history of headache including migraine may also be useful, as is a list of previous medications and response to them, including indomethacin and inhaled oxygen.

**Examination**

Generally, the neurological examination in SUNCT/SUNA is entirely normal between attacks. During an attack the cranial autonomic signs may be observed, but these abate quickly at the end of the attack. However, there is a minority of patients with abnormal interictal findings on examination, such as reduction of sensation or hyperesthesia to pinprick. Allodynia and hyperalgesia are also seen in all TACs, especially in those with migrainous comorbidity.

**Investigations**

MRI brain imaging is normal in the majority of cases, but may identify a pituitary or posterior fossa lesion that may be amenable to treatment and thus ameliorate the attacks of SUNCT/SUNA. If there are any abnormalities on neurological examination then an MRI is indicated, with dedicated trigeminal views if there is an abnormal sensation in the trigeminal nerve distribution. Blood tests including a pituitary profile may also indicate microprolactinoma that might not be apparent on brain MRI.

**Therapeutic Trials**

SUNCT may be differentiated from other TACs (especially in cases where groups of stabs cause seemingly longer attacks). Cluster headache responds well to high dose inhaled oxygen (100%, 12 l/min, for 15 min) as an acute abortive treatment, whereas SUNCT will not. Likewise, paroxysmal hemicrania (PH) is exquisitely responsive to indomethacin; therefore, a blinded modified indotest (100 mg indomethacin

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**Table 2** Symptomatic SUNCT/SUNA

<table>
<thead>
<tr>
<th>Location of lesion</th>
<th>Pituitary lesions</th>
<th>Posterior fossa</th>
<th>Local lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presumed mechanism of action</td>
<td>Via pituitary–hypothalamic axis</td>
<td>Local action on trigeminal nerve root or trigeminocervical complex or ascending pathways</td>
<td>Local action on trigeminal nerve</td>
</tr>
<tr>
<td>Examples</td>
<td>Macroadenomas</td>
<td>SUNCT: Arteriovenous malformations</td>
<td>Meningoencephalitis</td>
</tr>
<tr>
<td></td>
<td>Microadenomas</td>
<td>Brainstem cavernous hemangioma</td>
<td>Metastatic intraorbital carcinoid</td>
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<tr>
<td></td>
<td></td>
<td>Associated with HIV/AIDS</td>
<td>Associated with chronic sinusitis</td>
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<tr>
<td></td>
<td></td>
<td>Osteogenesis imperfecta</td>
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<tr>
<td></td>
<td></td>
<td>Craniosynostosis</td>
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<tr>
<td></td>
<td></td>
<td>Ischemic brainstem infarction</td>
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<tr>
<td></td>
<td></td>
<td>Pilocytic astrocytoma in V root entry zone</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Devic’s syndrome (neuromyelitis optica)</td>
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<tr>
<td></td>
<td></td>
<td>Plaque of multiple sclerosis in pons, cerebral peduncle, and the medulla</td>
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<tr>
<td></td>
<td></td>
<td>SUNA: Vertebral artery dissection</td>
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<tr>
<td></td>
<td></td>
<td>Pathological white matter changes in multiple sclerosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epidermoid cyst in cerebellopontine angle</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HIV/AIDS, human immunodeficiency virus/acquired immunodeficiency syndrome; SUNA, short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms; SUNCT, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.
intramuscularly, blinded against blinded 5 ml saline placebo) will be beneficial in PH but not SUNCT. A number of trials have demonstrated the effectiveness of intravenous lidocaine in SUNCT, which may aid in the diagnosis and also provide long-lasting benefit even after the infusion is stopped.

Treatment of SUNCT/SUNA

Treatment of SUNCT/SUNA is entirely aimed at preventive therapy, as the attacks are too frequent and short lasting for abortive therapy to be of any practical use.

Short-Term Preventive Medication

Short-term prevention in the form of intravenous lidocaine (1.3–3.3 mg/kg/h) is helpful to arrest the symptoms in hospital, although the side effects include cardiac arrhythmias and psychological disturbance. Therefore, the patient must have cardiac monitoring for the duration of the infusion, and the rate of infusion should be slowed if psychological adverse effects develop. Lidocaine can be given for up to 7 days, which may allow the patient at least some short-term relief from pain. Freedom from attacks has been reported up to 6 months after an infusion, but any length of remission may allow upward dose titration of a preventive medication.

Preventive Medication

Owing to the rare nature of these conditions and the severity of the symptoms making placebo a less attractive option, there is limited placebo-controlled trial data and, until recently, SUNCT and SUNA have been thought to be relatively refractory to treatment. There are a number of pharmacological agents that may be beneficial.

Lamotrigine

In open-label studies, lamotrigine given in doses up to 300 mg daily has been reported as highly efficacious in a number of series. In one series, the response to lamotrigine depended on the subtype of SUNCT, being more beneficial in episodic than chronic SUNCT. Side effects include a skin reaction that may progress to Stevens–Johnson syndrome.

Topiramate

Topiramate at doses up to 300 mg daily have proven beneficial in open-label studies of SUNCT, although the response in SUNA was less clear. Patients with a previous history of renal stones, glaucoma, or depression, and those who are underweight should not be offered topiramate as a first-line agent, in order to prevent these known side effects. Another adverse effect of topiramate is cognitive slowing, which can be minimized by starting at a low dose (12.5 mg) and increasing slowly (by 12.5–25 mg weekly or biweekly).

Gabapentin

Gabapentin at a dose of 800–2700 mg daily has been reported to show a good response in SUNCT in open-label trials. One trial suggested a better response in SUNA than in SUNCT, and thus gabapentin is suggested for use in SUNA, and as a second-line option in SUNCT.

Carbamazepine and oxcarbazepine

Carbamazepine at a dose of up to 900 mg daily has been shown to have a good or partial effect in SUNCT, although not in all patients. Generally carbamazepine is beneficial in trigeminal neuralgia, suggesting that the pathophysiology of SUNCT/SUNA is not entirely a peripheral trigeminal neuropathic process. There have been isolated reports of SUNCT responding to oxcarbazepine, and of a combination of oxcarbazepine and gabapentin.

Corticosteroids

Steroid treatment is used in the short-term preventive treatment of cluster headache, where it can allow upward titration of longer-use preventive medication. SUNCT and SUNA have not been thought to be responsive to steroid treatment in such form, but there is a series of patients with episodic SUNCT, who responded to oral methylprednisolone 1 mg/kg/day, for the duration of the bout, with good effect.

Treatment of Symptomatic SUNCT/SUNA

SUNCT/SUNA that is secondary to a structural lesion, either in the pituitary or posterior fossa, should respond to removal or treatment of the underlying cause. However, as previously described, treatment for pituitary adenomata, either with dopamine agonists or hypophysectomy, can either ameliorate or worsen the attacks. There are reports of SUNCT secondary to prolactinoma that were symptomatically treated either with conventionally described preventives such as lamotrigine or corticosteroids.

Nonsystemic Pharmacological Treatment

Greater occipital nerve (GON) injection: Subcutaneous injection of a combination of lidocaine and steroid in the region of the ipsilateral greater occipital nerve is effective in a range of headache syndromes, including migraine, cluster headache, paroxysmal hemicrania, and SUNCT. The mechanism is a neuromodulatory process affecting the trigeminocervical complex, thus affording relief of symptoms for weeks up to a few months, and therefore allowing the titration of preventive medications. The usual dose is 80 mg methylprednisolone combined with 2% lidocaine.

Non-Pharmalogical Interventions

Trigeminal microvascular decompression

Medically intractable SUNCT and SUNA cases with an aberrant arterial loop impinging on the trigeminal nerve at the root entry zone have benefited from microvascular decompression in a recent series, although symptoms may return after 9–32 months. Other cases of SUNCT have responded well to microvascular decompression of the arterial loops. Therefore, trigeminal microvascular decompression may be considered in patients with arterial loops impinging on the trigeminal nerve. This does not detract from the
hypothesis that SUNCT/SUNA is a centrally driven (probably hypothalamic) process, as the cranial autonomic symptoms are more prominent than in trigeminal neuralgia, and the impingement on the trigeminal nerve may act as a trigger to the attacks, rather like cutaneous stimuli such as touching the face.

**Occipital nerve stimulation**

Occipital nerve stimulation has been used in chronic migraine and cluster headache, and has been reported as effective in a series of SUNCT and SUNA patients, with a follow-up of up to 19 months. The mechanism is one of peripheral neuromodulation via the trigeminocervical complex, and is a relatively safe surgical option for treating medically intractable SUNCT/SUNA. Side effects are limited to local adverse effects of the surgery and implantation of the stimulator, although one patient subsequently developed hemicrania continua, which was treated with indomethacin.

**Deep brain stimulation**

Deep brain stimulation was targeted at the region of the posterior hypothalamus, following the functional imaging data that demonstrated activation in this region in SUNCT/SUNA, similar to cluster headache. There are a few cases of medically intractable SUNCT that have responded well to this treatment, being pain free for up to 18 months. Although the region of the posterior hypothalamus was targeted, more careful anatomical study has localized the target to the midbrain tegmentum. Adverse effects of deep brain stimulation, although not reported in these few cases of SUNCT, may include complications related to placement of the device, bleeding, and migration of the wires.

**Gamma knife radiosurgery**

Previously, gamma knife radiosurgery to the trigeminal nerve and sphenopalatine ganglion were considered to be unhelpful in SUNCT, and prone to significant adverse effects such as anesthesia dolorosa. However, there are recent reports in two cases of SUNCT that have responded well to this intervention.

**Summary**

SUNCT and SUNA are the rarest of the TACs, characterized by very brief, severe, painful attacks on one side of the face, usually orbital and retroorbital, with prominent ipsilateral cranial autonomic symptoms that must include both conjunctival injection and lacrimation in SUNCT, and either one, or neither, but not both, in SUNA.

The pathophysiology is suspected to be an abnormal activation in the region of the posterior hypothalamus, as in the other TACs, although there is also a peripheral component in terms of cutaneous triggering of attacks, which probably cause a physiologically abnormal response in the hypothalamic–trigeminal–autonomic connections.

SUNCT/SUNA are generally primary headache syndromes, but they are disproportionally represented in the literature of headaches secondary to the underlying structural causes. These most commonly include pituitary and posterior fossa lesions; therefore an MRI of the brain is recommended in their workup.

The differential diagnosis of SUNCT/SUNA includes other TACs; therefore therapeutic trials of oxygen and indomethacin, if negative, may help to rule out cluster headache and paroxysmal hemicranias, respectively.

Treatment is aimed at preventive care; short-term prevention includes intravenous lidocaine, and long-term preventive agents include lamotrigine, topiramate, gabapentin, and carbamazepine. Nonsystemic treatments such as GON injections are helpful, and the emergence of surgical options such as occipital nerve stimulation and deep brain stimulation may become more mainstream in the future treatment of medically intractable cases.

**See also:** Trigeminal Autonomic Cephalalgias (TACs) – Cluster Headache. Trigeminal Autonomic Cephalalgias (TACs) – Hemicrania Continua. Trigeminal Autonomic Cephalalgias (TACs) – Paroxysmal Hemicrania

**Further Reading**


**Relevant Websites**

http://ihs-classification.org/en/

International Headache Society Classification of SUNCT, SUNA and TACs.

www.uptodate.com

UpToDate: Clinical Articles on SUNCT and SUNA.