

Proposed practical working definitions of NORSE, FIRES, related syndromes, and Status Epilepticus (SE) of different severities: consensus panel

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Hotel Imlauer

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Objective

- To standardize terms, even if somewhat arbitrary or “semantic”
 - Allows multicenter studies
 - Improves communication, including via the literature
 - Gives a name to a clinical scenario/condition so that families can learn about it, and so that physicians know what to look up on the web, etc.
 - Helps with fundraising
- Identifying NORSE/FIRES early might help with treatment and identifying more specific diagnoses

The players:

- **Consensus team:**
 - 19 people from 8 countries; 7 pediatric—in red; * = attended the live consensus meeting in Salzburg (9 from 6 countries)
- *Lawrence Hirsch, USA [chair]
- *Nicolas Gaspard, Belgium
- *Andreas van Baalen, Germany
- *Rima Nabhout, France
- *Sophie Demeret, France
- *Tobias Loddenkemper, USA
- *Vincent Navarro, France
- *Nicola Specchio, Italy
- *Eugen Trinka, Austria
- Lieven Lagae, Belgium
- Andrea Rossetti, Switzerland
- Sara Hocker, USA
- Teneille Gofton, Canada
- Nicholas Abend, USA
- Emily Gilmore, USA
- Cecil Hahn, Canada
- Houman Khosravani, Canada
- Marissa Kellogg, USA
- Felix Rosenow, Germany

Proposed definition of NORSE

- New-Onset Refractory Status Epilepticus: A clinical presentation, in a patient without active epilepsy, with new onset of refractory status epilepticus without a clear acute or active structural, toxic or metabolic cause.
 - Most of the common acute or active structural, toxic or metabolic etiologies can be identified in the first few hours, but it may take up to 72h to rule out acute strokes, brain masses, drug overdoses, etc.
 - Includes viral infections; autoimmune syndromes of new onset, even if clear in the first 72h, e.g. classic anti-NMDA encephalitis; and allows remote brain injuries or resolved epilepsy.
 - Requires imaging, CSF analysis, toxicology and blood tests as recommended for evaluation of status epilepticus in other guidelines (e.g., Neurocritical Care Society).
 - Typically presents as super-refractory status epilepticus (SRSE), but this is not required for the diagnosis of NORSE.
 - Subgroup: Cryptogenic after extensive workup; referred to as “cryptogenic NORSE”.
 - Allows prior but resolved epilepsy due to possible coincidence of the two disorders.

Proposed definition of FIRES

- **FIRES: Febrile illness-related epilepsy syndrome**: a subcategory of NORSE that requires a prior febrile illness with fever starting between 2 weeks and 24h prior to onset of refractory status epilepticus.
 - Note: has to be refractory SE; no age cutoff; can be infant, child or adult.
 - Note: can be with or without fever at the time of onset of SE (about 50% have fever in prior literature)
 - Excludes most or all of febrile SE as fever in febrile SE is usually acute onset (few hours or less).

Proposed definition of IHHE:

- IHHE: Infantile Hemiconvulsion-Hemiplegia and Epilepsy syndrome:
A specific syndrome that presents as NORSE in a patient <2 years old, presenting with unilateral motor seizures, high grade fever at the time of onset of RSE, unilaterally abnormal acute imaging, followed by hemiparesis lasting at least 24h, and excluding infectious encephalitis.

SE of different severities: Definitions

- Refractory SE (RSE): SE persisting despite administration of at least 2 appropriate parenteral medications including a benzodiazepine. ■

Note: no specific duration required.

- Super-Refractory SE (SRSE): SE persisting at least 24 hours after onset, either without interruption despite appropriate treatment with anesthesia; recurring while on appropriate anesthetic treatment; or recurring after withdrawal of anesthesia and requiring its re-introduction.

- Prolonged SRSE (PSRSE): SRSE that persists or recurs after at least 7 days of appropriate treatment, including ongoing need for anesthetics.

- Prolonged RSE (PRSE): RSE that persists or recurs after at least 7 days of appropriate treatment, but without use of anesthetics.

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Let the investigations begin!

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WELCOME TO THE NORSE INSTITUTE

N.O.R.S.E. (New-Onset Refractory Status Epilepticus)



We strive to increase the awareness of NORSE, to stimulate, integrate, and support NORSE research, and to develop a shared community of NORSE researchers and families. Click below to browse our resources.

ADDENDUM, From ILAE paper (Trinka et al): Semiology Axis of classification:

- (A) *With prominent motor symptoms*
1. Convulsive SE (CSE, synonym: tonic–clonic SE)
 - a. Generalized convulsive
 - b. Focal onset evolving into bilateral convulsive SE
 - c. Unknown whether focal or generalized
 2. Myoclonic SE (prominent epileptic myoclonic jerks)
 - a. With coma
 - b. Without coma
 3. Focal motor
 - a. Repeated focal motor seizures (Jacksonian)
 - b. Epilepsia partialis continua (EPC)
 - c. Adversive status
 - d. Oculoclonic status
 - e. Ictal paresis (i.e., focal inhibitory SE)
 4. Tonic status
 5. Hyperkinetic SE

—cont-d—

(A) *Without prominent motor symptoms (i.e., nonconvulsive SE, NCSE)*

1. NCSE with coma (including so-called “subtle” SE)

2. NCSE without coma

a. Generalized

a. Typical absence status

b. Atypical absence status

c. Myoclonic absence status

b. Focal

a. Without impairment of consciousness (aura continua, with autonomic, sensory, visual, olfactory, gustatory, emotional/psychic/experiential, or auditory symptoms)

b. Aphasic status

c. With impaired consciousness

B.2.c Unknown whether focal or generalized

B.2.c.a Autonomic SE

NEW AND NOTEWORTHY

The first International NORSE and FIRES Symposium

Wednesday, April 5, 2017 1:30-5:30 pm

Hotel Imlauer & Bräu, Rainerstrasse 12-14, Salzburg, Austria

Symposium is free of charge. No registration is required.

Chairpersons: Rima Nababout and Nicolas Gaspard

Background, consensus definitions and hypotheses

- 1:30 Refractory Status Epilepticus of unknown cause: the nature of the problem. Nicolas Gaspard
- 2:00 NORSE/FIRES consensus definitions. Lawrence J. Hirsch
- 2:20 The NORSE-FIRES connection. Tobias Loddenkemper
- 2:40 FIRES: Pathophysiological hypotheses. Andreas van Baalen

Ongoing registries

- 3:00 Paratonnerre registry. Paratonnerre Scientific Committee
- 3:10 International NORSE registry. Nicolas Gaspard

Coffee Break

3:20 – 3:40

Clinical and research update

- 3:40 Immunotherapies: a systematic review of available evidence. Nicola Specchio
- 4:00 Preliminary findings from whole-exome sequencing. Giulia Barcia
- 4:20 Seizure semiology in FIRES. Raquel Farias-Moeller

Family issues

- 4:40 Communication of the NORSE/FIRES diagnosis. Nora Wong

Concluding remarks and Wine and Cheese Reception

5:00-5:30