Post-traumatic Confusion Case
Definition: Clinical Implications
and Use in Research

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ACRM BI-ISIG DOC Task Force
Confusion Group
Dr. Sherer has no significant financial relationships to disclose.
Learning Objectives

1. Upon completion, participant will be able to define the phenomenology and upper and lower boundaries of the post-traumatic confusional state.

2. Discuss recent literature that supports the definition of the post-traumatic confusional state.

3. Identify measures that could be used to assess the post-traumatic confusional state.
BI-ISIG DOC Task Force
Confusion Group Members

- Mark Sherer
- **Doug Katz**
- **Yelena Bodien**
- Cady Block
- Brian Greenwald
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- Risa Nakase-Richardson
- Shital Pavawalla
- Stuart Yablon
- Flora Hammond
- Don Stuss
Case Definition of Post-traumatic Confusion: Outline

- Background and motivation:
  - Where did the name Post-traumatic Confusional State come from?
  - How does PTCS differ from PTA or delirium?
  - How would a new case definition inform clinical and research practice?

- Process for reviewing and summarizing the evidence
  - Clinical questions
  - Literature search, abstract reviews, article reviews
  - Evidence tables
  - Literature search, abstract reviews, article reviews and evidence tables
  - Updated literature search, abstract reviews, article reviews and evidence tables with reassessment of the definition

- Integrating evidence and expert opinion
  - Delphi process
  - Three revisions and votes to reach consensus

- PTCS definition
- Key areas of discussion
W. Ritchie Russell (1903-1980)
Charles P. Symonds (1890-1978)

- Symonds, 1928: “clouded consciousness”
- Russell, 1932: “duration of loss of full consciousness” – retrospective report by patient of when he “woke up” “fully orientated and able to answer questions intelligently”
  - 200 patients: Longer duration associated with more neuro signs, more functional deficits, worse outcome (<1hr, 1-24hrs, 1-7d, >7d)
- Symonds & Russell, 1943: introduced term post-traumatic amnesia for this phenomenon
  - End-point: “beginning of continuous memory”
- Russell & Smith, 1961: “length of interval during which current events have not been stored”
Symonds, Mental Disorder Following Head Injury, Proc Royal Society of Medicine, 1937

- As the patient emerges from stupor he is, as a rule, excited, sometimes dazed and bewildered, and reacts in a resistive, irritable way to outside interference. Often there is delirium, sometimes with an occupational trend. This state may continue for days, weeks, or even months...

- Gradually, behaviour becomes quieter and speech more coherent, so that it is possible for short periods to engage the patient in conversation and learn something more of the mental content. The salient features at this stage are as follows:
  - profound disorientation in space and time, with a tendency to interpret the surroundings in terms of past experience
  - There is defect of perception and inability to synthesize perceptual data.
  - Memory and judgment are grossly impaired.
  - Thought is constantly impeded by perseveration
  - Disturbance of the speech function is conspicuous.
  - The mood is often elated and there is sometimes a push of talk resembling that seen in hypomanic states.
Post-traumatic amnesia
The Galveston Orientation and Amnesia Test (GOAT)

<table>
<thead>
<tr>
<th>Question</th>
<th>Error score</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is your name?</td>
<td>2</td>
<td>Must give both first name and surname.</td>
</tr>
<tr>
<td>When were you born?</td>
<td>4</td>
<td>Must give day, month, and year.</td>
</tr>
<tr>
<td>Where do you live?</td>
<td>4</td>
<td>Town is sufficient.</td>
</tr>
<tr>
<td>Where are you now?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) City</td>
<td>5</td>
<td>Must give actual town.</td>
</tr>
<tr>
<td>(b) Building</td>
<td>5</td>
<td>Usually in hospital or rehab center. Actual name necessary.</td>
</tr>
<tr>
<td>When were you admitted to this hospital?</td>
<td>5</td>
<td>Date.</td>
</tr>
<tr>
<td>How did you get here?</td>
<td>5</td>
<td>Mode of transport.</td>
</tr>
<tr>
<td>What is the first event you can remember after the</td>
<td>5</td>
<td>Any plausible event is sufficient (record answer).</td>
</tr>
<tr>
<td>injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can you give some detail?</td>
<td>5</td>
<td>Must give relevant detail.</td>
</tr>
<tr>
<td>Can you describe the last event you can recall</td>
<td>5</td>
<td>Any plausible event is sufficient (record answer).</td>
</tr>
<tr>
<td>before the accident?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>What time is it now?</td>
<td>5</td>
<td>1 for each half-hour error, etc.</td>
</tr>
<tr>
<td>What day of the week is it?</td>
<td>3</td>
<td>1 for each day error, etc.</td>
</tr>
<tr>
<td>What day of the month is it? (i.e. the date)</td>
<td>5</td>
<td>1 for each day error, etc.</td>
</tr>
<tr>
<td>What is the month?</td>
<td>15</td>
<td>5 for each month error, etc.</td>
</tr>
<tr>
<td>What is the year?</td>
<td>30</td>
<td>10 for each year error.</td>
</tr>
</tbody>
</table>

Total Error:

| 100 - total error | Can be a negative number. |

• **GOAT**
  - Emphasis on orientation
  - PTA cleared >75

• Other scales: e.g., Westmead PTA Scale, Orientation Group Monitoring System (OGMS), O-log
Donald T. Stuss

- Stuss & Buckle, JHTR, 1992: Acute period of recovery – PTA=hypoactive to hyperactive delirium: arousal and attention disorder coexisting with amnesia
- Stuss et al, J Neurosurg, 1999: Objective to characterize cognitive changes during acute period of recovery - emphasis on attention and memory
  - Conclusion: should call early period Posttraumatic confusional state instead of Posttraumatic amnesia
Stages of recovery from TBI (severe DAI)


**Rancho Scale**

1. Coma
2. Vegetative state (VS)
3. Minimally conscious state (MCS)
4. Confusional state/PTA (CS/PTA)
5. Post-confusional / emerging independence
6. Social competence / community reentry
7. Coma
8. Vegetative state (VS)
9. Minimally conscious state (MCS)
10. Confusional state/PTA (CS/PTA)
11. Post-confusional / emerging independence
12. Social competence / community reentry

**Braintree Neuro Stages**

**Def. transition / cognitive limitation**

- no arousal / unconscious
- Eye opening/sleep-wake / unconscious
- Simple, inconsist. signs awareness / imp. consciousness
- Resume interactive communic. or object use/ imp. attention, working mem., new learning
- Cleared PTA / imp. higher attention, retrieval, exec. func.
- Daytime household independence/ imp. exec. func., cog. speed , divided attention, memory efficiency, social awareness
M. Sherer et al.

- Nakase-Richardson et al., Prospective comparison of acute confusion severity with duration of post-traumatic amnesia in predicting employment outcome after traumatic brain injury. JNNP, 2007
- Sherer et al., Psychotic symptoms as manifestations of the posttraumatic confusional state: prevalence, risk factors, and association with outcome, JHTR, 2014
Possible Courses of Recovery after TBI

- Coma ➔ Vegetative State ➔ Minimally Conscious State ➔ Post-Traumatic Confusional State ➔ Continued Recovery
- Coma ➔ Minimally Conscious State ➔ Post-Traumatic Confusional State ➔ Continued Recovery
- Coma ➔ Post-Traumatic Confusional State ➔ Continued Recovery
- Post-Traumatic Confusional State ➔ Continued Recovery
- Altered consciousness
Motivations

• Define the DoC stage that follows MCS in patients with moderate to severe TBI and more prolonged DoC. (not just emerged from minimally conscious state - eMCS)

• PTA is not adequate to fully describe the syndrome/neurological condition (not just amnesia and disorientation)

• General definitions and diagnostic criteria for delirium are not fully specific or applicable to TBI
Why Is It Important to Have a Definition of the Post-traumatic Confusional State?

• To highlight the full syndrome seen in early recovery after TBI
• To facilitate improved clinical management of patients in PTCS
• To understand the implications of patterns of signs and symptoms of PTCS for recovery
• To allow investigation of how confusional state due to trauma is different from (or the same as) confusional state due to other disorders
Implications of Confusion for Clinical Management

- Patient safety
- Staff safety
- Supervision needs – staffing intensity
- Distress for family and close others
- Length of stay
- Discharge placement
- Long-term outcome
Process and Methods for Finding and Extracting Current Evidence:

Integrating Evidence with Expert Opinion
Clinical questions

• What is the phenomenology of PTCS?
• What is the lower boundary of PTCS?
• What is the upper boundary of PTCS?
• Do signs of PTCS recover in a particular pattern?
• How does functional status of persons in PTCS differ from persons who are no longer in PTCS?
• Is PTCS “time limited?”
• What is the pathophysiology of PTCS?
Process for Developing the Case Definition

1. Conducted literature search with key words (e.g., confusion, minimally conscious, minimally responsive, delirium, dementia, amnestic, etc.) (2013) – yielded 1757 abstracts
2. Reviewed abstracts in teams of 2 volunteers (retained 154 of 1757 abstracts)
3. Reviewed articles of retained abstracts, excluded some based on redefined criteria for inclusion – 53 article retained
4. Abstracted data in teams of 2 volunteers from 53 retained articles
5. Used abstracted data and evidence tables to further distill information for use in developing Delphi questions
6. Presented Delphi questions on 7 parts of the definition and held an initial vote (Galveston Brain Injury Conference, 2017)
7. Submitted parts of the definition that passed at Galveston for a vote by group members who did not attend Galveston
Process for Developing the Case Definition

8. Revised parts of the definition that did not pass at Galveston and submitted for a group vote (3 revisions and 3 votes to reach consensus)
9. Updated literature review to include publications from 2013-2017 – yielded 649 abstracts
10. Abstracts rated and reconciled by 2 reviewers. Retained 6 articles.
11. Data extracted from 6 retained articles and evidence tables updated
12. Met in-person to address manuscript preparation (Galveston 2018)
13. Collated all articles previously marked for “query”- to determine their utility for the current paper
14. Reviewed articles for references not captured on the prior literature searches but suggested by the group as being potentially relevant (retained 10 articles from 60 abstracts)

Total Abstracts Reviewed = 2,466
Total Articles Reviewed = 181
Total Articles Abstracted = 69
<table>
<thead>
<tr>
<th>Process for Developing the Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013 – February 2016</td>
</tr>
<tr>
<td>Literature Search</td>
</tr>
<tr>
<td>March 2016</td>
</tr>
<tr>
<td>Evidence Tables</td>
</tr>
<tr>
<td>May-December 2017</td>
</tr>
<tr>
<td>Delphi Votes 1-3 to accept definition</td>
</tr>
<tr>
<td>March 2018</td>
</tr>
<tr>
<td>2013-2017 Updated Abstract and Article Review</td>
</tr>
<tr>
<td>April 2018</td>
</tr>
<tr>
<td>Updated Evidence Tables based on 2013-2017 Review</td>
</tr>
<tr>
<td>May 2018</td>
</tr>
<tr>
<td>Developed Manuscript Outline</td>
</tr>
<tr>
<td>June-August 2018</td>
</tr>
<tr>
<td>Abstract and Article Review of Additional Research</td>
</tr>
<tr>
<td>August-present 2018</td>
</tr>
<tr>
<td>Manuscript Prep</td>
</tr>
</tbody>
</table>
Number of Articles by Topic
<table>
<thead>
<tr>
<th>Reference</th>
<th>Key Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baird, Papadopoulou, Greenwood, et al., 2005</td>
<td>45% of subjects without PTA had attention impairment; subjects with PTA (per GOAT) were not assessed (attention=speed of processing via Trails A/B).</td>
</tr>
<tr>
<td>De Monte, Geffen, Massavelli, et al., 2006</td>
<td>Mild TBI patients in PTA transcribed fewer symbols than mild TBI patients not in PTA; the non-PTA cohort scored as non-impaired (attention=speed of processing via digit symbol test). PTA=5 questions from Rapid Screen for Concussion+3 additional questions</td>
</tr>
<tr>
<td>Kennedy, Nakase-Thompson, Nick, et al., 2003</td>
<td>Attention, memory, orientation, comprehension, vigilance were associated with delirium but only vigilance stood out when odds ratios were adjusted. (attention=visual span from WAIS III and vigilance=auditory sustained attention task) All subjects level IV or above on Rancho Los Amigos Scale; Cognitive test of delirium vs DSM IV criteria</td>
</tr>
<tr>
<td>Nakase-Richardson, Yablon, Sherer, et al., 2007</td>
<td>91% of patients who met clinical delirium diagnostic criteria had an attention impairment on the attention rating item of the Delirium Rating Scale-Revised (attention= 0-3 scale from alert/attentive to severe difficulty focusing and/or sustaining attention); 47% who did not meet delirium diagnostic criteria had attention impairment</td>
</tr>
<tr>
<td>Reference</td>
<td>Key Finding</td>
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<tr>
<td>-----------</td>
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</tr>
<tr>
<td>Baird, Papadopoulou, Greenwood, et al., 2005</td>
<td>73% of patients without PTA (per GOAT) had memory impairment but patients with PTA were not assessed. Of those, 74% had severe memory impairment. (memory=Recognition Memory Tests for words and faces)</td>
</tr>
<tr>
<td>De Monte, Geffen, Massavelli, et al., 2006</td>
<td>Mild TBI patients in PTA had poorer performance on a 5-world learning task (on the learning and delay trials) than patients with mild TBI not in PTA, however no group differences were found for immediate recall test; the non-PTA cohort scored as non-impaired (memory= word list from SAC); PTA=5 questions from Rapid Screen for Concussion+3 additional questions</td>
</tr>
<tr>
<td>Ewert, Levin, Watson, et al., 1989</td>
<td>All patients started in PTA (GOAT); procedural memory improved during PTA, declarative memory did not (procedural memory= mirror reading, Porteus maze, Pursuit Rotor, Recognition Memory Test; declarative memory=declarative memory questions)</td>
</tr>
<tr>
<td>Kalmar, Novack, Nakase-Richardson, et al., 2008</td>
<td>Patients in PTA (32% of total sample) more impaired than patients not in PTA on all CVLT tasks; PTA=GOAT TBIMS criteria</td>
</tr>
<tr>
<td>Reference</td>
<td>Key Finding</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Kennedy, Nakase-Thompson, Nick, Sherer, 2003</td>
<td>Severity of disorientation as measured by the Cognitive Test for Delirium was predictive of a clinical diagnosis of delirium in a sample of 65 persons with TBI</td>
</tr>
<tr>
<td>McCrea, Kelly, Randolph, et al., 2002</td>
<td>15 athletes who experienced LOC and/or PTA of 91 who sustained concussion showed poorer orientation on the Structured Assessment of Concussion than athletes who did not sustain concussion or compared to their pre-concussion, baseline scores; PTA=inability to recall events immediately after the injury for no more than 24 hours</td>
</tr>
<tr>
<td>Sherer, Yablom, Nakase-Richardson, 2009</td>
<td>Approximately 95 of 107 confused patients showed disorientation as measured by the GOAT on their initial assessment after admission for rehabilitation</td>
</tr>
</tbody>
</table>
PTCS: phenomenology, symptom fluctuation

Total Articles: 7

<table>
<thead>
<tr>
<th>Reference</th>
<th>Key Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakase-Richardson, Yablon, Sherer, 2007</td>
<td>91% of 78 patients making a clinical diagnosis of delirium showed fluctuation on the Delirium Rating Scale – Revised as compared to only 21% of 93 patients not in delirium</td>
</tr>
<tr>
<td>Sherer, Yablon, Nakase-Richardson, 2009</td>
<td>Fluctuation was present for 41 of 41 patients with severe confusion as assessed by the CAP, 28 of 28 patients with moderate confusion, and 37 of 38 patients with mild confusion on initial assessments after admission to rehabilitation</td>
</tr>
<tr>
<td>Ewert, Levin, Watson, Kalisky, 1989</td>
<td>11 of 16 patients in PTA by GOAT criteria showed fluctuation in GOAT scores across 4 assessments where fluctuation was indicated by any decrease in GOAT score on a subsequent assessment</td>
</tr>
</tbody>
</table>
Sources of Information to Guide Creation of a Case Definition

- **Empirical investigations**
  - Vary by quality of evidence
  - Limited to a few aspects of the overall condition

- **Expert opinion**
  - Depends on prior experience and practice setting of experts
  - May be difficult to achieve consensus among experts
Consensus process

• Delphi Technique:
  – Iterative feedback process
  – Participants receive feedback of the position of the whole group, summation of comments, range of opinions, reasons underlying and the participant’s own position.
  – Group tends to converge towards a consensus with each iteration.
  – Consensus achieved when reach a target threshold of agreement (e.g., 80%)
The Case Definition for the Post-Traumatic Confusional State
The post-traumatic confusional state is a disorder of consciousness characterized by the following core neurobehavioral features:

A. Disturbances of Attention: reduced ability to focus or sustain attention.
B. Disorientation: impaired orientation to place, time and situation.
C. Disturbances of Memory: impaired ability to encode and recall new information.
D. Fluctuation: The character and severity of the disturbance waxes and wanes during the course of the day.
PTCS Case Definition Part 2:

Identifying the core clinical features of PTCS requires systematic serial assessment, recognizing that these features vary in severity and improve at different rates as the condition evolves.
PTCS Case Definition Part 3: Phenomenology

In addition to these four core neurobehavioral features, PTCS can include any of the following:

A. Emotional and/or behavioral disturbances: including but not limited to agitation/restlessness and/or hypoactivity; irritability, impulsivity, disinhibition, aggression and/or decreased responsiveness; affective lability and/or flattening.

B. Sleep-wake cycle disturbance: excessive sleep, insufficient sleep, alteration of normal sleep pattern, or decreased level of arousal.

C. Confabulation: false memory

D. Delusions: fixed false beliefs

E. Perceptual disturbances: illusions, hallucinations.
Impairments in the core and associated areas are of sufficient severity to limit functional independence and interfere with the individual’s ability to cooperate with needed medical care, maintain personal safety, and/or interact effectively with others and the environment.
The core and associated features are not better explained by another preexisting, established, or evolving neurocognitive disorder, psychiatric disorder, medical condition, substance intoxication or withdrawal, or exposure to a toxin or medication.
PTCS can occur as a condition immediately after trauma or as a transition from a lower or higher level of consciousness. For those individuals who transition from a lower level of consciousness, such as coma, VS/UWS or MCS, the lower boundary of the PTCS is characterized by recovery of at least basic functional communication and/or simple, meaningful environmental interactions. The period of transition can be indistinct or fluctuating in some patients.
Emergence from PTCS is defined by clinically important improvement in the four core and associated neurobehavioral features as demonstrated by:

A. Ability to attend to and process simple information so that the individual is able to cooperate with caregivers by following instructions and attending when performing basic familiar tasks,
B. General orientation to time, place, and personal circumstances,
C. Ability to recall some recent events or learn at least limited new information that can be recalled later, and
D. Lack of marked cognitive or behavioral fluctuations so that the patient can participate in simple social interactions.

A portion of individuals will have more severe persisting problems in one or more cognitive domains that inform the diagnosis of the residual clinical condition (e.g. aphasia, amnesia).
Examples of Measures to Assess PTCS

- No current measures of delirium/confusion address all features of the case definition
- Not enough data to endorse specific measures

<table>
<thead>
<tr>
<th>Construct</th>
<th>CAP</th>
<th>DRS-R98</th>
<th>CAM</th>
<th>TOTART</th>
<th>NBRS</th>
<th>GOAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>P</td>
<td>O</td>
<td>O</td>
<td>P</td>
<td>O</td>
<td>NA</td>
</tr>
<tr>
<td>Memory</td>
<td>P</td>
<td>O</td>
<td>O</td>
<td>P</td>
<td>NA</td>
<td>P</td>
</tr>
<tr>
<td>Disorientation</td>
<td>P</td>
<td>O</td>
<td>O</td>
<td>P</td>
<td>O</td>
<td>P</td>
</tr>
<tr>
<td>Symptom fluctuation</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Behavioral disturbance</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>NA</td>
<td>O</td>
<td>NA</td>
</tr>
<tr>
<td>Sleep-wake cycle disturbance</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>NA</td>
<td>O</td>
<td>NA</td>
</tr>
<tr>
<td>Confabulation</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Delusions</td>
<td>O</td>
<td>O</td>
<td>NA</td>
<td>NA</td>
<td>O</td>
<td>NA</td>
</tr>
<tr>
<td>Perceptual disturbance</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>NA</td>
<td>O</td>
<td>NA</td>
</tr>
</tbody>
</table>

P=performance-based   O=observational   NA=not assessed
Assessment Issues for PTCS

• Should diagnosis of PTCS be obtained by clinical exam or by a systematic set of measures?
• Should measures be performance measures, rating scales, or a combination of both?
• Who is qualified to assess PTCS?
• Should assessments address functional abilities or just areas of cognitive or neurobehavioral impairment?
• When should assessment for PTCS begin and end in a patient’s course of recovery?
• How often should assessments be completed?
Questions for PTCS Research

- How is confusion (delirium) after TBI similar to and different from deliria from other causes?
- Are there subtypes of confusion after TBI or does severity of confusion account for most of the variability?
- What is the time-course of PTCS?
- What are the neuroanatomical and pathophysiologic factors that underlie confusion?
- How can the case definition be translated to a reliable and valid clinical diagnostic instrument?
- What environmental and behavioral approaches are most effective in managing PTCS?
- Are the any pharmacologic interventions that can ameliorate some as aspects of PTCS without worsening others?
Thank you!