

Post-Traumatic Confusional State

Afik Faerman, Ph.D.

Adapted with permission from:

Yelena Bodien, Ph.D., Doug Katz, Ph.D., Mark Sherer, Ph.D.

BI-ISIG DoC Task Force Confusion









Disclosures

• Dr. Faerman has no significant financial relationships to disclose with regards to the current projects.



Post-Traumatic Amnesia

- Charles P. Symonds (1890-1978), 1928: "clouded consciousness"
- W. Ritchie Russell (1903-1980), 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 posttraumatic amnesia for this phenomenon,
 - + End-point defined as the "beginning of continuous memory"
- Russell & Smith, 1961: "length of interval during which current events have not been stored"

LANCET] AIR-COMMODORE SYMONDS, MAJOR RUSSELL: ACCIDENTAL HEAD INJURIES [JAN. 2, 1943 7

ACCIDENTAL HEAD INJURIES not control in the

PROGNOSIS IN SERVICE PATIENTS

C. P. SYMONDS W. RITCHIE RUSSELL MD EDIN, FRCPE, MRCP MAJOR, RAMC

THE word accidental in the title of this paper requires xplanation. In the course of our work at a military spital for head injuries we have had to deal with two ups of cases-gunshot or bomb wounds, and a variety thead injuries due to accidents of a kind which may lso occur in civil life. It is with this latter group that present paper is concerned. There is much uncernty among surgeons and physicians regarding the prognosis in these cases, as is shown by the great variety pinion expressed on the optimum duration of rest bed, the period of convalescence required, and the lihood of return to useful duty in the Services. With he aid of a grant from the Medical Research Counci have been able to collect data which have a bearing a these problems, and at the suggestion of the council's experience and conclusions.

Cases of accidental head injury admitted to this hospital may be divided into two groups. (1) Chronic cases which have been previously treated in other hospitals; many of these have been transferred because their progress, judged by expectation, has been unsatisfactory, and they therefore form a highly selected group. (2) Acute, cases; a relatively unselected group, being usually admitted because the accident happened in the neighbourhood of the hospital, though many had been transferred. Cases admitted to this hospital within 3 weeks of the injury have been included in the acute group. The series is thus not entirely representative of accidental injuries, such as would be seen in a large general hospital in an industrial area, because it does not include those cases in which the severity of the head injury, or associated injuries of other parts, forbade transfer within the period specified. Doubtless this explains why the number of deaths in our series was

The analysis covers 242 consecutive acute cases; 5 died, and 22 (9%) of the survivors were invalided out of the Service from this hospital. The remainder, 215 (88%), were returned to duty, and it is with the subsequent fate of this group that we are first concerned.

POST-TRAUMATIC AMNESIA IN ACUTE CASE

One of us has previously emphasised that a convenient ans of classifying the severity of head injuries is the ration of the post-traumatic amnesia (Russell 1932).
is method is incomplete, because it takes no account of local injury to the skull, brain or cranial nerves, but is useful provided these limitations are clearly recog-Post-traumatic amnesia is taken to end at the me from which the patient can give a clear and consecuaccount of what was happening around him. This be estimated by careful questioning after recovery of full consciousness and normal orientation. Care is sary to avoid two sources of error. One arises om accepting the patient's first memory of his surround ags as the end-point, when it has in fact been followed by a further period of clouded consciousness and amnesia. Such "islands" of memory are not uncommon and may be followed by further amnesia for a day or : it is therefore the beginning of continuous memor we prefer as our measurement. The second ugh less common, error is to assume that because a nt is aware of what is happening around him he will be able to recall this later. This may lead to underestimation of the duration of the post-traumatic lesia in a patient who is under observation in the te stage of his symptoms. It is therefore necessary ses of this type to check the duration of the amnesia ome time after the apparent recovery of full conscious-ess, for example, before the patient is discharged from

In table I the prognosis in those who survived is compared with the duration of the post-traumatic amnesia (PTA). Of the 215 cases returned to duty, 193 (90%) have been followed up, and the table gives

not only the number of those invalided from the Service in this hospital but also of those known to have relapsed and been invalided later. The figures show that as the duration of the PTA lengthens the prognosis becomes worse. There is a rise in the proportion of those winvalided when the PTA exceeds 1 day, and a further significant rise in the over 7 days group. But a third of the most severe cases (PTA over 7 days) returned to duty successfully, and at the other end of the scale, of those with a PTA of less than 1 hour (including those with no amnesia), 11% were invalided. This table, therefore, indicates both the value and the limitations

TABLE I—SURVIVING ACUTE CASES: PROGNOSIS IN RELATION TO SEVERITY OF INJURY

Duration of PTA	Cases	Invalided in hosp.	Invalided later	Total invalided	No follow-up
Nil	28	1 (4%)	2 (7%)	3 (11%)	1
Under 1 hour	75	2 (3%)	6 (8%)	8 (11%)	9
1-24 hours	65	3 (5%)	5 (8%	8 (12%)	7
1-7 days	34	5 (15%)	3 (9%)	8 (24%)	2
Over 7 days	35	11 (31%)	10 (29%)	21 (60%)	3
Total	237	22 (9%)	26 (11%)	48 (20%)	22 (9%)

Percentages are of the number in each subgroup.

of the duration of the PTA as a criterion of prognosis. All that can be said for it is that it is the best single criterion at present available.

A record of the type of duty performed was included in the follow-up questionnaire, and the proportion of those on duty who were reported to be on full duty, efficiently performed, was 829°. This did not, however, always indicate that the patient was still in the same medical category as before the accident.

DURATION OF HOSPITAL TREATMENT AND REHABILITATION

The plan has been to continue with treatment in hospital, including graduated physical exercise, until the patient is ambulant and then to transfer him to a convalescent hospital nearby; there, supervised by the medical officer who had charge of him in hospital, he is given physical training of progressive severity, and mental occupation, until he is judged fit for return to duty.

to duty.

Of 193 cases discharged to duty and successfully followed up, 167 were reported on duty. Table II gives the actual duration of treatment and rehabilitation of those who returned to duty successfully: 92% were treated for less than 3 months, and of these, 84% were reported by the medical officer of the unit to be doing full duty efficiently. On the other hand, 26 patients were

TABLE II-DURATION OF TREATMENT IN ACUTE CASES WITH A SATISFACTORY FOLLOW-UP REPORT AFTER RETURN TO DUTY

Months from in- jury to discharge to duty		Duration of post-traumatic amnesia							
		Nii	Under 1 hr.	1-24 hr.	1-7 days	Over 7 days	Total		
Under ‡		4 (4)	4 (3)	nu şa i	Spinore (22)	10 1999	8 (7)		
Over 1		7 (7)	20 (20)	10 (10)	1 (1)	THE TO	38 (38)		
1-2		7 (6)	19 (19)	23 (19)	15 (12)	1 (0)	65 (56)		
2-3	701	6 (5)	13 (10)	12 (6)	5 (3)	7 (4)	43 (28)		
3-4	1	hud.	2 (0)	3 (2)	1 (1)	1 (0)	7 (3)		
4-5		1.2.	district	2 (2)	2 (1)	1(1)	5 (4)		
5-6				name :	son Beta	1 (1)	1 (1)		
Over 6		\$ 9/13 H	os se		and the	1.4	19.00		
Total	bo.	24 (22)	58 (52)	50 (39)	24 (18)	11 (6)	167 (137)		

Figures in parentheses show patients doing full duty efficiently.

Duration of treatment (including rehabilitation) was less than 3 months in 154 cases (92%); of these, 129 were doing full duty efficiently.

Post-Traumatic Amnesia

- Symonds, C. P. (1937). Mental disorder following head injury:
 - + "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, behavior 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 (Testing)

- GOAT
- Emphasis on orientation
- PTA cleared >75
- Other scales: e.g., Westmead PTA Scale, Orientation Group Monitoring System (OGMS), O-log

The Galveston Orientation and Amnesia Test (GOAT)

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

76-100 = Normal 66-75 = Borderline < 66 = Impaired

(Levin et al., 1979)

Post-Traumatic Amnesia

Stuss & Buckle, JHTR, 1992: Acute period of recovery

PTA = hypoactive to hyperactive delirium: arousal and attention disorder coexisting with amnesia

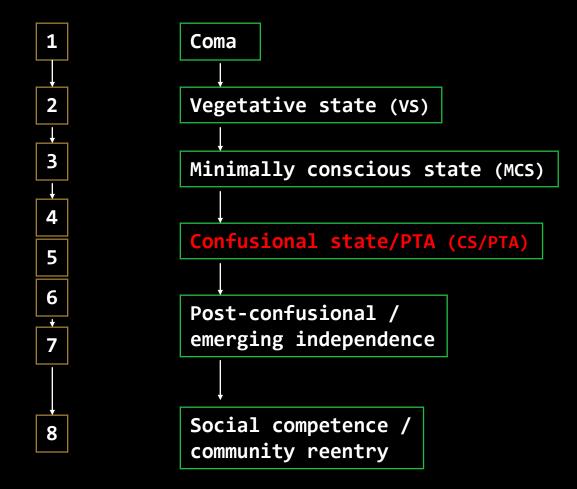
Stuss et al., J Neurosurg,
1999: Objective to
characterize cognitive
changes during acute period
of recovery - emphasis on
attention and memory

Conclusion: should call early period posttraumatic confusional state instead of Posttraumatic amnesia

Stages of recovery from TBI

Rancho Scale Braintree Neuro Stages

Def. transition / cognitive limitation



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Tye 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.
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Daytime household independence/ imp. exec. func., cog. speed , divided attention, memory efficiency, social awareness

Evidence for Attentional Impairment

- Nakase-Thompson et al, Acute confusion following traumatic brain injury. Brain Injury, 2004
- Sherer et al, Multidimensional assessment of acute confusion after traumatic brain injury. Arch Phys Med Rehab, 2005
- 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, Effect of severity of post-traumatic confusion and its constituents symptoms on outcome after traumatic brain injury. Arch Phys Med Rehabil, 2008
- Sherer et al., Patterns of recovery of posttraumatic confusional state in neurorehabilitation admissions after traumatic brain injury. Arch Phys Med Rehabil, 2009
- 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

Continuous altered consciousness

Motivation

- 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



Importance of Definition



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

Clinical Risk of Confusion

- Patient safety
- Staff safety
- Supervision needs staffing intensity
- Distress for family and close others
- Length of stay
- Discharge placement
- Long-term outcome
- Any other ideas?



What is the phenomenology of PTCS?

What is the lower boundary of PTCS?

What is the upper boundary of PTCS?

Is PTCS "time
 limited?"

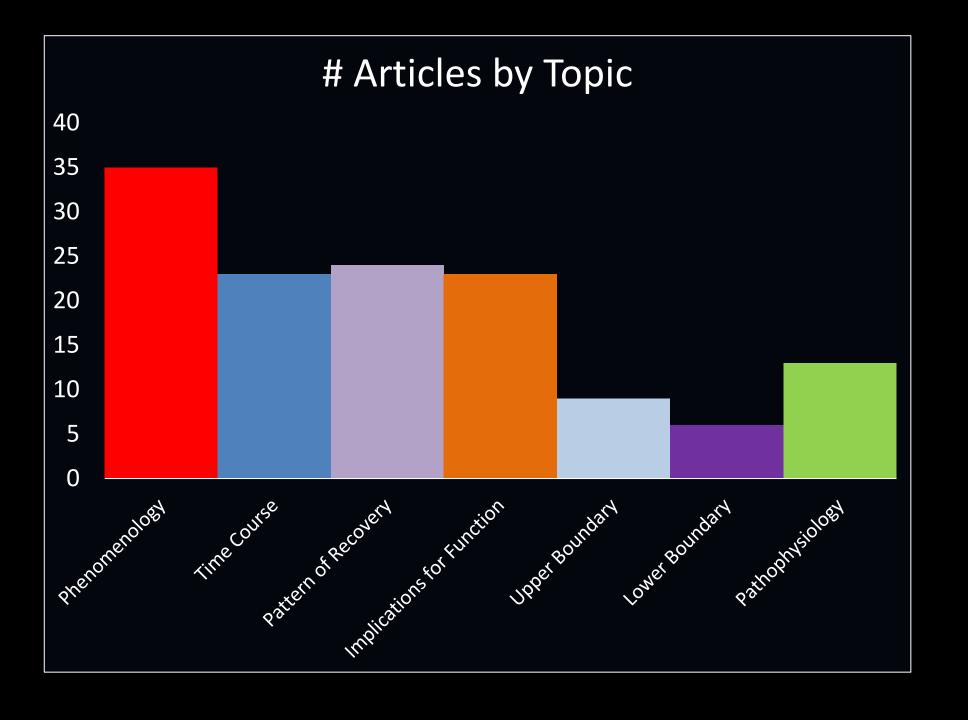
Do signs of PTCS recover in a particular pattern?

How does functional status of persons in PTCS differ from persons who are no longer in PTCS?

What is the pathophysiology of PTCS?

Developing the Case Definition

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



PTCS: phenomenology, attention

Reference	Key Finding
Baird, Papadopoulou, Greenwood, et al., 2005	45% of subjects without PTA had attention impairment; subjects with PTA (per GOAT) were not assessed (attention=speed of processing via Trails A/B).
De Monte, Geffen, Massavelli, et al., 2006	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
Kennedy, Nakase- Thompson, Nick, et al., 2003	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
Nakase-Richardson, Yablon, Sherer, et al., 2007	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

PTCS: phenomenology, memory

Reference	Key Finding
Baird, Papadopoulou, Greenwood, et al., 2005	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)
De Monte, Geffen, Massavelli, et al., 2006	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
Ewert, Levin, Watson, et al., 1989	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)
Kalmar, Novack, Nakase- Richardson, et al., 2008	Patients in PTA (32% of total sample) more impaired than patients not in PTA on all CVLT tasks; PTA=GOAT TBIMS criteria

PTCS: phenomenology, orientation

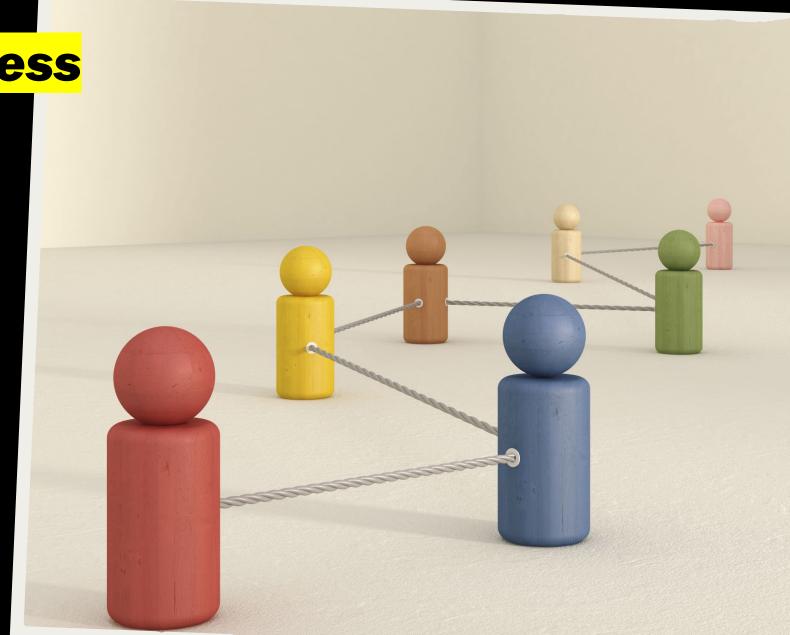
Reference	Key Finding
Kennedy, Nakase- Thompson, Nick, Sherer, 2003	Severity of disorientation as measured by the Cognitive Test for Delirium was predictive of a clinical diagnosis of delirium in a sample of 65 persons with TBI
McCrea, Kelly, Randolph, et al., 2002	15 athletes who experienced LOC and/or 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
Sherer, Yablon, Nakase- Richardson, 2009	Approximately 95 of 107 confused patients showed disorientation as measured by the GOAT on their initial assessment after admission for rehabilitation

PTCS: phenomenology, symptom fluctuation

Reference	Key Finding
Nakase-Richardson, Yablon, Sherer, 2007	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
Sherer, Yablon, Nakase- Richardson, 2009	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
Ewert, Levin, Watson, Kalisky, 1989	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

Consensus Process

- Delphi Technique:
 - + 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%)



Guides for 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

1. Phenomenology Assessment

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.
- 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.

(Sherer et al., 2020, APMR)

2. Phenomenology

In addition to these 4 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.Delusions: fixed false beliefs
- D. Perceptual disturbance: illusions, hallucinations
- E.Confabulation: false memory

(Sherer et al., 2020, APMR)

2. Functional Implications

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.

4. Differential Diagnosis

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.

5. Lower Boundary

PTCS can occur 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/unresponsive wakefulness syndrome, 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.

6. Upper Boundary

Emergence from PTCS is defined by clinically important improvement in the 4 core and associated neurobehavioral features as demonstrated by the following:

- 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
- 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 1 or more cognitive domains that inform the diagnosis of the residual clinical condition (e.g., aphasia, amnesia).

(Sherer et al., 2020, APMR)

How to assess PTCS?

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

Construct	САР	DRS-R98	CAM	TOTART	NBRS	GOAT
Attention	Р	0	0	Р	0	NA
Memory	Р	0	0	Р	NA	Р
Disorientation	Р	0	0	Р	0	Р
Symptom fluctuation	0	0	0	NA	NA	NA
Behavioral disturbance	0	0	0	NA	0	NA
Sleep-wake cycle disturbance	0	0	0	NA	0	NA
Confabulation	NA	NA	NA	NA	NA	NA
Delusions	0	0	NA	NA	0	NA
Perceptual disturbance	0	0	0	NA	0	NA

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?

Project #2: Biomarker Identification

Open Questions from Project #1

- 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?

Identifying

Biomarkers of PTCS

- A scoping review
- Using PICOT questioning model:
 - + Patient / Population /
 Problem
 - + Intervention
 - + Comparison
 - + Outcome
 - + Timeframe



PICOT Questions

- 1. For patients with traumatic brain injury, do biomarkers, such as structural imaging, functional imaging, electrophysiological procedures, protein biomarkers, genetic markers, differentiate patients with PTCS/PTA from those who are not in PTCS?
- 2. For patients in a confusional state/delirium, do biomarkers, such as structural imaging, functional imaging, electrophysiological procedures, protein biomarkers, genetic markers differentiate patients with PTCS resulting from TBI from those with PTCS from other conditions who are evaluated with the same biomarkers?

PICOT Questions

- 3. For patients in a confusional state after traumatic brain injury, are biomarkers, such as structural imaging, functional imaging, electrophysiological procedures, protein biomarkers, genetic markers, associated with different levels of severity or durations of PTCS?
- 4. For patients in a confusional state after TBI, are biomarkers, such as structural imaging, functional imaging, electrophysiological procedures, protein biomarkers, genetic markers, obtained during PTCS, associated with cognitive or functional outcome?
- 5. For patients in a confusional state after TBI, do biomarkers together with measures of severity/duration of PTCS predict cognitive or functional outcome better than either alone?

Current status

- 3036 abstracts identified
- 70 full text reviewed
- 36 articles retained
- TBD for full relevant PICOT information
- Planned to be updated with recent literature



Thank You

Yelena Bodien, Ph.D.



Doug Katz, Ph.D.



Focus Group:

- + Mark Sherer
- + Keira Hays
- + Bei Zhang
- + Amy Rosenbaum
- + Yelena Bogdanova
- + Michael Marino
- + Brigid Dwyer
- + Julie
- + Sonja Blum
- + Emma-Jane Mallas
- + Min Graf
- + Michael Williams



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SPECIAL INTEREST GROUP