Intensive Care Med (2017) 43:223–225
DOI 10.1007/s00134-016-4550-x

WHAT'S NEW IN INTENSIVE CARE

What's new in cognitive function in ICU survivors

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Increasing numbers of patients survive a critical care admission, but many of them develop morbidities, including cognitive impairments, that have devastating consequences. Cognitive impairment affects 10–62 % of ICU survivors, with most studies reporting deficits in a third to half of patients [1]. Variability in the prevalence of cognitive impairments across studies is explained by heterogeneity in assessments (questionnaires, cognitive screening tests, or neuropsychological test batteries) and variable follow-up intervals [1]. While some patients have prior cognitive impairment, critical illness results in de novo cognitive deficits in previously healthy individuals. New or worsening cognitive impairment appears more prevalent in the critically ill than in other hospitalized patients. For example, one study found significantly higher odds of cognitive impairment after severe sepsis, compared to hospitalized patients without sepsis [2]. It is unclear if a "dose response" exists pertaining to the relationship between severity of illness and severity of cognitive impairment, although numerous studies have found that traditional markers of illness severity are not predictive of cognitive deficits or cognitive decline.

Cognitive impairments occur regardless of diagnosis on admission to the ICU. In cases of profound critical illness such as ARDS and sepsis, cognitive impairments occur in 20–56 % of ARDS survivors [3] and 16–40 % of patients with sepsis [4]. A large prospective cohort study found 40 % of ICU survivors had cognitive impairments comparable to cognitive impairments in patients with moderate traumatic brain injury or mild Alzheimer's disease [5].

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Post-ICU cognitive impairments occur in the domains of attention, processing speed, memory, and executive function, but important other domains, such as language, have received less study. Cognitive impairments across multiple domains suggest that critical illness results in diffuse brain injury. Neuroimaging findings include global and focal atrophy, cortical and subcortical lesions, lesions in the corpus callosum, hippocampus, basal ganglia, superior frontal lobes, and widely distributed white matter lesions [6].

Several mechanisms of critical illness-related brain injury have been identified (Fig. 1) but additional research is needed [7]. Risk factors for cognitive impairment include patient characteristics such as prior psychological disorders, acute stress in the ICU, or older age (Fig. 1), rather than characteristic markers of illness severity such as APACHE II score or ICU length of stay. While older individuals are most vulnerable, cognitive impairments are prevalent among children [8] and young, middle-aged, and older adults [5, 9]. Finally, chronic health conditions (e.g., COPD, diabetes) and pre-existing cognitive impairment can influence cognitive outcomes post-ICU. Acute conditions such as pneumonia also increase the risk of cognitive decline; alternatively small changes in cognitive function increase the risk of pneumonia [10]. Studies are needed to characterize and understand pre-illness risk factors of cognitive impairment, such as smoking, obesity, and APOE genotype, and whether such risk factors are modifiable.

Trajectories of cognitive functioning after critical illness are heterogeneous and under-researched. Trajectories may include (1) continuation of premorbid cognitive function, (2) cognitive impairment that improves to the pre-ICU level of function, (3) cognitive impairment that improves but not to the pre-ICU level, (4) cognitive impairment that does not change over time, and (5) cognitive impairment that initiates a cascade of events

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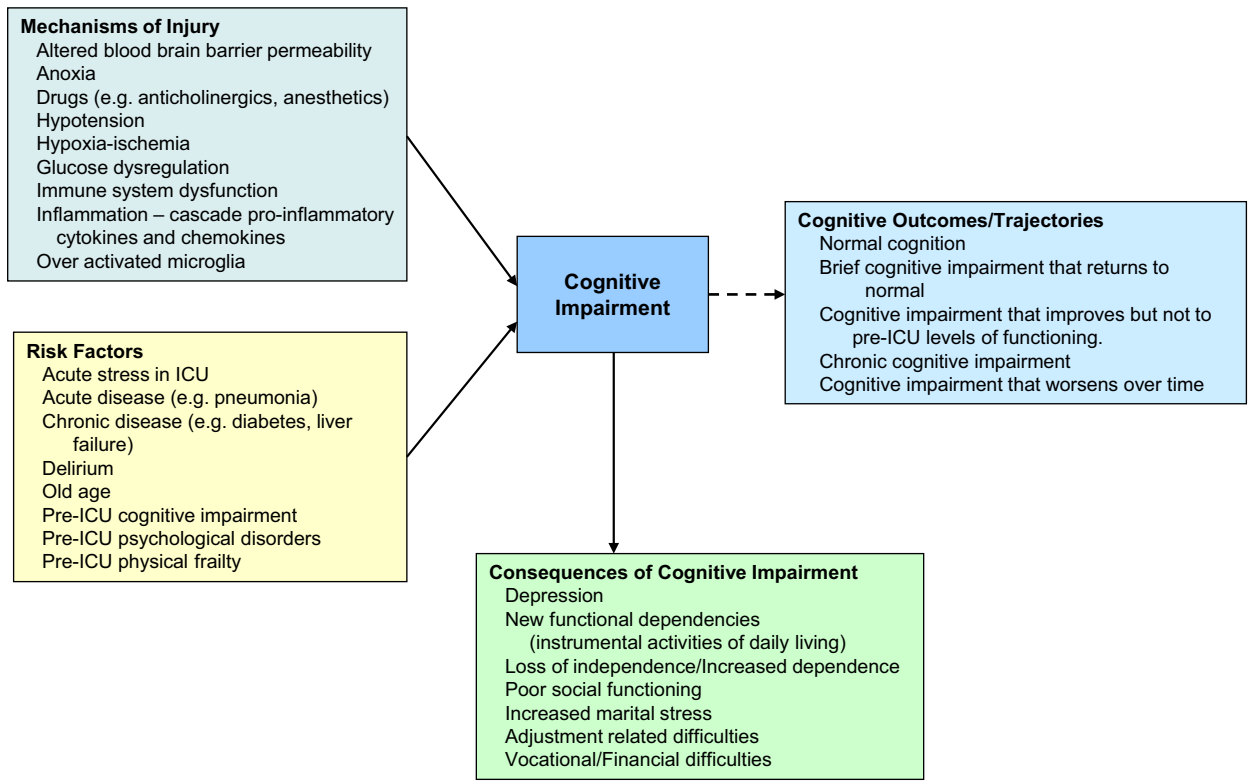

Fig. 1 Mechanisms of brain injury (*light-green box*) and risk factors (*yellow box*) associated with development of cognitive impairments, and adverse consequences of cognitive impairment for patients and their families (*green box*). The *dashed line* show possible cognitive outcome trajectories (*light blue box*)

resulting in a worsening over time (Fig. 1). Large longitudinal studies are needed to determine trajectories.

Like cognitive impairment, psychological morbidity [e.g., post-traumatic stress disorder (PTSD), depression, or anxiety] is prevalent among ICU survivors. Psychological morbidity may be associated with brain injury as well as psychosocial factors. Meta-analyses demonstrate that both depression and PTSD are associated with an array of cognitive deficits in domains including psychomotor speed, attention, memory, and executive functioning. Neuroimaging studies reveal neuronal loss, including hippocampal atrophy, in some patients with depression or PTSD. However, the relationships between psychological and cognitive problems among ICU survivors is unclear. As is the case in the general population, it is uncertain if psychological disorders are comorbid with cognitive impairment, cause cognitive impairment, or if psychological disorders are caused or worsened by cognitive impairment. For example one study found higher depression in ICU survivors with cognitive deficits [11] but another detected no relationship between depression or anxiety and post-ICU cognitive impairment [12].

Poor cognitive outcomes predict impairments in instrumental activities of daily living (e.g., financial and medication management, or problems driving, shopping) [13], loss of independence, poor social functioning and adjustment, and unfavorable financial consequences. Among individuals who were working before ICU admission, only about 50 % return to work. A longitudinal study found employment post-ICU improved over time, with 49 % of individuals employed at 1 year increasing to 77 % at 5 years. However the patients were relatively young (median age of 44 years) [14] and as such these findings may not generalize to other ICU populations. Individuals with physical morbidity, ongoing health concerns, and cognitive impairment are particularly unlikely to return to work. Studies that assess return to work probably underestimate the scope of the problem, as many individuals may return to work but in a reduced or "under-employed" capacity.

Given the high rate of post-ICU cognitive impairments and their profound consequences, interventions to prevent or ameliorate cognitive impairments are essential. In-ICU interventions such as reducing narcotics,

sedatives, and delirium, improving sleep architecture, providing psychological support, promoting early mobility, and making recovery plans are key. Given the liberal use of systemic corticosteroids in the ICU, their potentially injurious effects on the brain need to be studied. Post-ICU interventions should include continuing psychological support, and physical and cognitive rehabilitation. Benefits of such an approach are demonstrated by a study that found combined cognitive and physical therapy improved executive function and instrumental activities of daily living compared to patients who received usual care [15].

Cognitive impairment is a serious problem, with devastating consequences for ICU patients and their families, which needs increased recognition and action from both clinicians and researchers. As clinicians, we need to educate patients and families about post-ICU outcomes, guiding and supporting them in pursuit of their goals and outcome priorities. "Big data" and translational studies are needed to understand mechanisms of injury, risk factors, and trajectories of cognitive impairment after critical illness, while interventions to prevent or improve cognitive outcomes should be urgently evaluated. It is essential that ICU clinicians think not only about survival but also about the longitudinal effects of critical illness/interventions on patient outcomes.

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Acknowledgments
Dorothy Wade receives funding from the National Institute for Health Research (NIHR) UCL Hospitals Biomedical Research Centre.

Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflict of interest.

Received: 25 July 2016 Accepted: 11 September 2016
Published online: 30 September 2016

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