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## IDENTIFYING THE THERAPEUTIC WINDOW; THE ISSUE OF TIMESCALES IN CLINICAL VERSUS EXPERIMENTAL TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) is one of the most complex human diseases involving dynamically changing pathologies such as altered metabolism, inflammation, cell death, etc. Experimental TBI, using mostly rodents has developed several successful evidence-based treatments that significantly improved the outcome of injured animals. These treatments however have only been poorly, if at all are translated into the clinic. As therapies can only be efficient when administered during their specific therapeutic window, our current lack of understanding of how rodent and human timescales are related can significantly contribute to the failure of translating effective therapies from the bench to the bedside. The timescales of basic biological processes such as enzyme kinetics are comparable between species. More complex physiological processes, e.g., gestation, sexual maturation and lifespan however run on vastly different timescales in rodents than in humans. Similarly, as recent evidence has demonstrated a ''rat day'' is not equivalent to a human day when it comes to complex pathologies, such as sepsis and inflammation.
In order to improve translating successful experimental treatments into successful treatments of TBI patients, we will compare the rodent and human timescales of major pathologies in experimental vs. clinical TBI. We then review existing ''best practices'' in clinical and experimental TBI with emphasis on the timescales of monitoring changes of various biomarkers so can we generate experimental data comparable to clinical timescales. Finally, we will address the feasibility and the potential of developing algorithms converting existing temporal data between rodent and human TBI studies.

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## MINIMAL BRAIN INJURY: LONG-TERM NEUROPSYCHIATRIC CONSEQUENCES

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Minimal Brain Injury (MBI) is defined as Glasgow Coma Scale (GCS) score of 15, normal findings on neurologic examination in emergency room, and negative findings on head computed tomographic (CT) scan.
The purpose was to evaluate the neuropsychiatric consequences in 15 adults (11 men and 4 women) aged 23 to 30, after 3 years of MBI as result of car accident. They had a GCS score of 15 - no loss of consciousness (LOC) or amnesia - and negative findings on CT upon evaluation in emergency room. Besides this: no previous psychiatric and neurologic disorders, head injury, substance abuse history. All patients were employed, and no one developed posttraumatic stress disorder after injury.
Patients were diagnosed by Schedules for Clinical Assessment in Neuropsychiatry and free detailed clinical interview. Signs and symptoms were compatible with DCR-10, ICD-10 and DSM-5.
Patients presented a combination of organic mood (affective) disorders, organic anxiety disorder, mild cognitive disorder, intermittent explosive disorder and oppositional defiant disorder.
This study presents certain limitations: it is retrospective with a limited number of patients, showing a specific subpopulation of head injured patients.
It is important to note that the criterion was limiting. The disorders, according to the free detailed clinical interview, were present long ago but had not been diagnosed. My study was retrospective, and I specifically examined patients with delayed injury rather than acute patients.
This research supports a main conclusion: physical trauma need not be great to cause adverse psychiatric disorders, even in individuals who have stable backgrounds.

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## EFFECT OF CYCLOPHILIN D KNOCK-OUT ON DIFFERENT SUBDOMAINS OF TRAUMATICALLY INJURED AXONS

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Genetic deletion of Cyclophilin D (CypD) reduces formation of the mitochondrial permeability transition pore. We have previously used APP immunohistochemistry to demonstrate that this deletion reduces axonal pathology in the mouse neocortex following central fluid percussion injury (cFPI). We now extend this work to enable pathological