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Markov Blankets and Cognitive Dysfunction in mTBI: Insights from Simulation Models

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Abstract: *Mild Traumatic Brain Injury (mTBI) is a prevalent neurological condition that can lead to persistent cognitive impairments, disrupting memory, attention, and executive function. In this study, we explore the mechanisms of cognitive decline in mTBI through the lens of Markov blankets—a theoretical framework that delineates the statistical boundary between the brain's internal and external states. By simulating the impact of mTBI on sensory, active, internal, and external states, we demonstrate how disruptions to the Markov blanket structure contribute to impairments in predictive coding and cognitive processing. Our simulation introduces noise and connectivity reductions that mimic the neurometabolic and synaptic changes following mTBI, revealing delayed sensory processing, impaired motor function, and cognitive instability. These findings highlight the importance of Markov blankets in maintaining cognitive integrity and offer novel insights into the pathophysiology of post-concussion syndrome. Understanding how mTBI disrupts the brain's functional architecture through Markov blanket disturbances may inform more effective diagnostic and therapeutic approaches.*

Keywords: *mild traumatic brain injury; markov blankets; cognitive impairment; simulation; predictive coding; post-concussion syndrome*

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1. Introduction

Mild traumatic brain injury (mTBI) represents a considerable public health issue, impacting millions of people globally each year. Although the majority of individuals recover fully within a few weeks, a significant portion of patients suffer from ongoing cognitive impairments that can adversely affect their quality of life (Mavroudis et al., 2022).

The Mayo classification system characterizes mTBI as a brain injury that results from a sudden impact or jolt to the head (Malec et al., 2007). Typically, individuals diagnosed with mTBI present with a Glasgow Coma Scale (GCS) score between 13 and 15, a loss of consciousness lasting less than 30 minutes, and post-traumatic amnesia that persists for less than 24 hours (Malec et al., 2007). Symptoms associated with mild TBI can endure for days, weeks, or even months, often leading to substantial disruptions in daily activities. Cognitive impairments following mTBI are diverse, encompassing deficits in various cognitive domains as well as increased emotional distress and somatic complaints (McInnes et al., 2017). Numerous studies have focused on the cognitive profile of mTBI patients during the acute phase, revealing significant impairments in global cognition, executive functions, and episodic memory (de Freitas Cardoso et al., 2019; McCrea et al., 2014). A key pathological feature of TBI, including mTBI, is diffuse axonal injury (DAI). This condition arises when the shearing forces involved in the injury cause damage to axons. The severity of DAI is directly correlated with the intensity of the deceleration force, and it can be detected within hours of the traumatic event. DAI is believed to be a critical factor contributing to early cognitive impairments following mTBI (Spain et al., 2010; Dikmen et al., 2001).

2. Cognitive Impairment in mTBI

The duration and severity of cognitive impairment following a mild traumatic brain injury (mTBI) can vary significantly, influenced by individual differences and the specifics of the injury. Research has demonstrated that cognitive impairments, along-side associated white matter damage, can not only emerge in the immediate aftermath of an mTBI but may also persist for several years post-injury (Miller et al., 2001). Cognitive assessments conducted at intervals of one month and twelve months post-injury consistently reveal deficits in individuals who sustained a mild TBI, as indicated by Glasgow Coma Scale (GCS) scores ranging from 13 to 15 (Carroll et al., 2004). Moreover, psychological factors such as de-pression and anxiety are strongly correlated with diminished cognitive performance, especially in cases where the mTBI is complicated or progresses toward more severe forms of injury, with these effects being particularly notable one year after the injury (Nordström et al., 2013). This persistence of cognitive deficits underscores the necessity for ongoing monitoring and evaluation of cognitive functions in individuals who have experienced mTBI.

Cognitive impairments post-mTBI can manifest in several forms, including global cognitive dysfunction, impaired executive function, and episodic memory deficits. These impairments can be acute, occurring within the first few days after the injury, but may also transition into chronic issues, affecting attention, working memory, decision-making, and reaction times over extended periods (Rabinowitz et al., 2020). Subjective cognitive de-cline, where individuals perceive a reduction in their cognitive abilities, even in the absence of objective test abnormalities, can also be a chronic consequence of mTBI, further complicating recovery and quality of life (Nelson et al., 2016).

Additionally, the severity and duration of cognitive impairments after mTBI are influenced by a range of factors, including the individual's age, level of education, socioeconomic status, and any prior history of traumatic brain injuries. For instance, older adults tend to experience more pronounced cognitive declines post-mTBI, particularly in areas such as processing speed, working memory, and attention, with these deficits being exacerbated by lower cognitive reserve and the presence of other medical conditions (Nelson et al., 2016; Covassin). Depression and anxiety, common comorbidities in individuals with mTBI, further exacerbate cognitive impairments by

affecting brain structure and function, particularly in networks involved in cognitive processing (Crane et al., 2016). These psychological conditions can hinder cognitive recovery by impairing attention, memory, and other cognitive functions, thereby contributing to prolonged cognitive deficits (Kroes et al., 2011).

3. Brain Areas Involved in Cognitive Decline After mTBI

Research exploring the brain regions implicated in cognitive decline following mild traumatic brain injury (mTBI) has identified significant disruptions in functional connectivity networks as a predictor of cognitive impairments during the acute phase of mTBI (Dunkley et al., 2015). Early cognitive impairments have been linked to changes in the organization of critical brain networks, such as the rich-club organization, which is involved in efficient information processing across the brain (Alhourani et al., 2016). Additionally, alterations in low-frequency connectivity within large-scale brain networks have been shown to predict the long-term cognitive sequelae of mTBI, with particular emphasis on disrup-tions within the default mode networka network crucial for memory and attention functions (Irimia et al., 2022). Disruptions in this network are particularly associated with attention deficits, a common cognitive dysfunction following mTBI (Bruineberg, Kiverstein, & Rietveld, 2016). Furthermore, white matter changes, especially those near cerebral microbleeds, have been correlated with age and sex-dependent cognitive decline post-mTBI (D'Souza et al., 2020).

4. Markov Blankets in the Brain

The concept of Markov blankets, originally introduced by Judea Pearl in 1998 in the context of statistical inference, has become a significant framework for under-standing the organization of systems, particularly in neuroscience (Pearl et al., 1998). A Markov blanket refers to a set of states that mediate the interaction between internal states of a system and their external environment, effectively separating these two domains through a layer of 'blanket' states. This partition consists of sensory states, which in-fluence internal states but are not influenced by them, and active states, which influence external states but are not influenced by them. This configuration establishes conditional independence between internal and external states, a key feature for main-taining the integrity of the system under varying conditions (Friston et al., 2013).

In the context of the brain, Markov blankets do not correspond to physical boundaries like cell membranes but rather to statistical partitions that define which variables within the brain are conditionally independent from others. This construct has been applied to describe the dynamics of neuronal and cognitive processes without necessarily implying a physical boundary but rather highlighting functional distinctions within the brain's operational architecture (Hipólito et al., 2021). The debate continues as to whether Markov blankets should be interpreted literally or instrumentally—whether they describe actual physical processes in the brain or serve as a useful abstraction for understanding neuronal and cognitive activities (Hipólito et al., 2021; Andrews et al., 2020).

A Markov blanket in the brain can be mathematically defined as the set of variables that render internal states (denoted as $\mu\mu$) conditionally independent from external states (denoted as $\eta\eta$). The relationship between these states can be expressed through the factorization of their joint probability distribution, showing that internal and external states interact only through the blanket states, thereby maintaining the system's conditional independence (Kirchhoff et al., 2018). This structure is particularly relevant in dy-namic systems, such as the brain, where the interactions among states are constantly evolving.

Within neuronal circuits, Markov blankets can be identified at various levels of organization. For instance, at the level of individual neurons, the internal states (such as ion channel conductance) are distinct from the external states (like synaptic inputs from other neurons), with blanket states mediating their interactions. This allows neu-rons to change their activity in response to inputs

without losing their identity, pre-serving the system's integrity across different functional states (David et al., 2003). The dynamics of these interactions are captured by equations that describe how internal states evolve based on the influences of both internal and blanket states, while external states influ-ence sensory and active states (David et al., 2003).

At larger scales, such as cortical microcircuits, the concept of Markov blankets helps to describe the interactions between different populations of neurons. Here, the internal states might correspond to specific neural activities within a column, while the blanket states mediate interactions between different columns. This framework has been particularly useful in understanding the hierarchical organization of the brain, where sensory and active states facilitate communication between different layers and regions, integrating top-down and bottom-up processing streams (Bastos et al., 2012). The Markov blanket structure not only supports the brain's ability to process information efficiently but also underpins the brain's capacity for self-organization and adaptability, ensuring that it can maintain functional coherence under changing conditions (Friston, 2019).

Markov blankets are also pivotal in understanding how larger brain networks in-teract. Brain-wide networks can be conceptualized as higher-order assemblies of neu-ral units, each wrapped in their own Markov blankets.

These networks interact with one another through mechanisms that preserve the conditional independence of internal states within each network, while facilitating communication across different networks. This nesting of blankets across different scalesfrom individual neurons to entire brain networksprovides a framework for understanding the brain as a complex, selforganizing system (Bilek et al., 2020).

The model could inform diagnostics by helping clinicians better understand the disruptions in cognitive processes following mTBI. Additionally, the framework could be utilized in rehabilitation strategies by guiding targeted interventions, personalizing treatments based on the specific cognitive dysfunctions observed in patients. Integrating these practical applications would significantly enhance the impact and applicability of your theoretical insights.

5. Markov Blankets in Active Inference and Predictive Coding

The concept of a Markov blanket serves as a statistical boundary that separates internal states from external states, allowing for conditional independence between the two. This partitioning of states into internal and external, mediated by sensory and active states, establishes the framework for how the brain can interact with its environment while maintaining internal integrity. A Markov blanket ensures that internal states influence external states only through active states, while external states influence internal states only through sensory states. This conditional independence forms the foundation for understanding the dynamics of systems like the brain in terms of active inference (Beal et al., 2003).

A simple example to illustrate this is a living cell, which relies on its Markov blanket to maintain its boundary from the surrounding environment. If the Markov blanket of a cell deteriorates, the cell would cease to exist, as it would no longer be distinguishable from the external environment (Hohwy, 2017). Thus, the identity of any biological system is predicated on the presence of a Markov blanket, making it a fundamental concept for understanding self-organization in living systems.

Active inference refers to the process by which biological systems, through their internal and active states, minimize uncertainty about their environment to maintain their structural and functional integrity. This is achieved by continuously engaging with the external environment through sensory and active states. The structure of a Markov blanket allows internal and external states to influence each other in a reciprocal manner through sensory and active states, effectively supporting the system's ability to engage in active inference. The core of active inference is based on minimiz-ing surprise or uncertainty about sensory states, which drives an organism toward re-ducing the free energy in its interactions with the environment (Friston Et al., 2015; Anderson, 2017).

The principle of free energy minimization underpins active inference. According to the free energy principle, organisms must minimize variational free energy to maintain their integrity. Free energy is a measure of the difference between the organ-ism's internal model of the world and the actual sensory inputs it receives. Minimizing this discrepancy allows the organism to make more accurate predictions about its en-vironment and ensure its continued existence by reducing surprise (Beal, 2003). This process of minimizing free energy is equivalent to Bayesian inference, where the organism con-tinuously updates its beliefs about the world based on sensory evidence.

In the brain, active inference and free energy minimization are closely tied to the framework of predictive coding. Predictive coding posits that the brain operates as a hierarchical system, making predictions about sensory inputs and minimizing prediction errors. The Markov blanket at each level of the brain's hierarchy separates active states, which influence lower levels, from sensory states, which propagate prediction errors up the hierarchy. This continuous exchange between prediction and error cor-rection allows the brain to fine-tune its internal model, thereby maintaining coherence between its internal states and the external environment (Anderson, 2017; Bruineberg et al., 2016).

At each level of the brain's hierarchy, the Markov blanket facilitates the interac-tion between internal and external states by ensuring that sensory states convey pre-diction errors to higher levels, while active states modify predictions at lower levels. This hierarchical structure allows the brain to minimize free energy across different scales, from basic sensory processing to higher-order cognitive functions. By minimiz-ing prediction errors at every level, the brain engages in active inference, continuously refining its model of the world to reduce uncertainty and ensure the organism's survival (Hohwy, 2012).

Markov blankets play a crucial role in active inference and predictive coding, al-lowing the brain to interact with the environment in a way that minimizes surprise and uncertainty. Through the process of free energy minimization, organisms use sen-sory and active states to maintain their structural and functional integrity, ensuring that their internal models of the world align with the external realities they encounter.

6. Markov blankets and memory in cognitive systems

Markov blankets serve as a crucial framework for understanding how systems, such as cognitive systems, maintain separation between internal and external states. This statistical separation allows different parts of a system to maintain distinct roles, such as memory, which would be impossible in a homogeneous system without distinct parts. For this separation to be sustained over time, a steady-state distribution is required, ensuring that internal and external states remain statistically distinct. Howev-er, there appears to be a contradiction: cognitive systems like ours, which possess memory, rely on shared information between internal and external states, seemingly contradicting the conditional independence that Markov blankets impose (Squire, 2004).

This apparent contradiction is resolved by understanding that a system does not remain in a steady state but evolves toward a steady-state density. Once initial condi-tions, such as a past memory, are imposed, the system temporarily deviates from this steady-state density, meaning that transient dependencies between internal and ex-ternal states can occur. These transient synchronizations between internal and exter-nal states are part of the memory process, during which past states influence current states through the blanket, before the system returns to a steady state. This mechanism explains how memory can exist within Markov blanketed systems, even though the system as a whole is driven toward conditional independence between internal and external states over time (Cavanagh et al., 2020).

Memory can be quantified using tools from information theory, information ge-ometry, and dynamical systems theory. The time course of memory-related changes varies according to different factors, such as the solenoidal and dissipative gradient flows within the system and the variance of internal and external state densities. These measures demonstrate that transient violations of

conditional independence in Markov blanketed systems are not limited to simple stochastic processes but apply to a wide variety of systems, including cognitive ones (Bliss and Lomo, 1973).

In cognitive systems, memory is generally divided into short-term and long-term categories (Squire, 2004). Both forms of memory involve temporary deviations from the condi-tional independence imposed by Markov blankets. Short-term memory, particularly working memory, allows a cognitive system to hold information temporarily for on-going cognitive tasks, such as planning or decision-making (Baddeley, 2003). This type of memory often involves regions like the prefrontal cortex, where neural activity persists longer than in sensory regions, maintaining dependencies between internal and external states over short periods (Kiebel et al., 2008; Hasson et al., 2008).

In a typical working memory experiment, a stimulus is presented, removed, and then recalled after a delay. The external state is represented by the stimulus, and the internal state is the neural representation that persists during the delay, guiding the appropriate response when prompted. During this delay, conditional dependencies between internal and external states must be maintained to ensure correct task per-formance, demonstrating how working memory functions within the framework of a Markov blanket (Astle et al., 2009; Lepsien and Nobre, 2007; Lepsien et al., 2011; Fuster, 1973; Barceló et al., 2000).

Long-term memory, on the other hand, is often classified into declarative (explic-it) and non-declarative (implicit) forms (Squire and Zola, 1998; Anderson, 1976). Declarative memory includes episodic and semantic memory, while non-declarative memory encompasses procedural memory, such as learned motor skills. These long-term memories involve more sus-tained deviations from the steady-state density, where associations between internal and external states persist over long periods, often years. Procedural memory, for in-stance, involves the gradual synchronization of external motor patterns with internal neural states over repeated actions, such as learning to reach or perform a task (Adolph and Franchak, 2017; Soliveri et al., 1992; Ackermann et al., 1996; Molinari et al., 1997; Tseng et al., 2007; Huerta and Rabinovich, 2004; Friston and Herreros, 2016).

Episodic memory, a type of declarative memory, involves spatiotemporal associa-tions, such as remembering an event in a specific place and time. This form of memory depends on structures like hippocampal place and time cells, which encode relation-ships between locations and temporal sequences. In contrast, semantic memory in-volves associations without spatiotemporal context, such as the relationship between a word and its meaning. Both types of memory involve conditional dependencies be-tween internal states (e.g., neural representations) and external states (e.g., environ-mental cues) (Eichenbaum, 2014; O'Keefe and Dostrovsky, 1971).

The distinction between short-term and long-term memory can be understood in terms of the time it takes for conditional dependencies between internal and external states to dissipate. Short-term memory involves faster transitions back to conditional independence, while long-term memory involves more persistent deviations. These temporal dynamics reflect the physiological differences in the systems supporting each type of memory, such as the faster neural time constants for short-term memory and the slower changes in synaptic efficacy associated with long-term memory (Cavanagh et al., 2020; Bliss and Lomo, 1973).

7. Pathophysiology of concussion

7.1. Acute Neurometabolic Cascade

Concussion triggers an immediate disturbance in cellular homeostasis through mechanical forces, resulting in a complex neurometabolic cascade. This process begins with "mechanoporation," a disruption of the cell membrane, causing an outflow of in-tracellular potassium and widespread neuronal depolarization (Steenerson et al., 2017). This event leads to a diffuse depression of neuronal activity, similar to mechanisms seen in migraines, and contributes to the immediate clinical symptoms of concussion (Giza and Hovda, 2014).

The release of excitatory neurotransmitters, such as glutamate, further exacer-bates the situation by promoting potassium efflux via ligand-gated channels and acti-vating N-methyl-D-aspartate (NMDA) receptors, resulting in a feedback loop of depo-larization and hyperexcitability (Mc Fie et al., 2018; Giza and Hovda, 2001). Animal studies have shown that glutamate levels spike immediately post-injury but typically normalize within hours (Yi and Hazell, 2006). In con-trast, human studies have demonstrated region-specific alterations in both glutamate and gamma-aminobutyric acid (GABA) levels, particularly in the dorsolateral pre-frontal cortex (DLPFC), where changes persist for days to weeks post-concussion (Yasen et al., 2018). This suggests that these neurometabolic disruptions are time-dependent and specific to particular brain regions.

Concussive injuries also cause intracellular calcium accumulation, driven by glu-tamate release, leading to mitochondrial impairment and, in some cases, cell damage (Cheng et al., 2012; Barkhoudarian et al., 2011). This metabolic disturbance is compounded by genetic factors, such as muta-tions in the CACNA1A gene, which are associated with prolonged recovery and more severe post-concussion symptoms (Terwindt et. Al, 2022; McDevitt, 2016).

7.2. Energy Crisis

Restoring ionic homeostasis after a concussion places a high metabolic demand on the brain. Following the initial injury, animal studies have shown a 30-46% increase in neuronal glycolysis within the first 30 minutes, which can persist for up to six hours (Yoshino et al., 1991). This hypermetabolic phase is then followed by a period of glucose hypometabo-lism lasting 5 to 10 days, during which oxidative metabolism remains inefficient, leading to anaerobic processes and lactate accumulation (Kawamata et al., 1995; Kalimo et al., 1981). In humans, this metabolic pattern has been observed using fluorodeoxyglucose (FDG)-PET imaging, revealing post-injury hyperglycolysis followed by a hypometabolic phase, particularly in veterans with repeated head injuries (Peskind et al., 2011).

The "window of vulnerability," a period of heightened risk for further injury due to metabolic instability, underscores the importance of cautious post-injury management (Prins et al., 2013; DeFord et al., 2002). During this time, the brain is more susceptible to the detrimental effects of a second impact, although the exact duration of this vulnerability remains to be fully de-fined.

7.3. Blood Flow and Neurovascular Changes

Concussion-induced changes in cerebral blood flow (CBF) are hypothesized to follow a triphasic (hypo-hyper-hypo) pattern, although data on mTBI is limited (Fidan et al., 2018). Autoregulatory and vasoreactive disturbances are believed to drive these changes, as shown in animal models where significant decreases in global and regional CBF are observed post-injury (Martin et al., 1997). In human studies, MRI-based measurements have shown reduced CBF in key brain areas, such as the frontal and temporal lobes, and in regions involved in autonomic regulation and emotion processing (e.g., the cingulate cortex, insula, and hippocampus) during the first week post-concussion (Choe et al., 2012).

Although some studies have not found significant decreases in CBF compared to controls, trends toward reduced CBF velocity in the immediate post-injury period sug-gest that further research is warranted to fully understand the hemodynamic changes associated with concussion (Thibeault et al., 2018). These blood flow alterations may correlate with symptom severity and tend to normalize more slowly than clinical symptoms, indi-cating that neurovascular recovery lags behind the resolution of cognitive deficits (Wang et al., 2016; Meier et al., 2015).

7.4. Axonal and Cytoskeletal Injury

The mechanical forces of a concussion cause neuronal shearing, which results in microstructural axonal damage. This injury disrupts axonal transport and leads to the accumulation of beta-amyloid precursor protein (b-APP) in neurons, a hallmark of axonal injury in traumatic brain injury (TBI) (Choe et al., 2012). Calcium influx following the injury further destabilizes microtubules, leading to additional cytoskeletal damage (Johnson et al., 2103; Nixon, 1993).

Although diffuse axonal injury (DAI) is more commonly associated with severe TBI, it is also present across the spectrum of TBIs, including concussions (Choe et al., 2016). Animal models have shown that unmyelinated axons in immature brains are particularly vul-nerable to damage, especially when subjected to repeated mTBI (Prins et al., 2011; Reeves et al., 2005). This vulnera-bility has been further demonstrated in studies where repeated concussions lead to significant neurochemical and white matter changes, as evidenced by decreased frac-tional anisotropy (FA) in the corpus callosum and hippocampus (Fidan et al., 2018).

7.5. Impaired Synaptic Plasticity

Synaptic plasticity, the brain's ability to adapt and remodel neural connections, is impaired following concussion. Animal studies have demonstrated that mTBI disrupts normal synaptic activity, including changes in NMDA receptor function and GABA-ergic interneurons, which are essential for maintaining synaptic balance (Rabinowitz & Watanabe, 2020). These disruptions affect long-term potentiation (LTP), a key process in learning and memory, and can persist for days to weeks after injury (White et al., 2017).

7.6. Neuroinflammation

Neuroinflammation, marked by the activation of microglia and the release of in-flammatory cytokines such as interleukin 1β (IL-1B) and interleukin 6 (IL-6), is a significant factor in the pathophysiology of concussion (Rathbone et al., 2015). This inflammatory response, driven by the breakdown of the blood-brain barrier (BBB) and the infiltration of pe-ripheral immune cells, can lead to ongoing cellular damage and may contribute to the persistence of post-concussive symptoms (Loane and Byrnes, 2010).

Evidence suggests that individuals with elevated levels of inflammatory markers, such as high-sensitivity C-reactive protein (hsCRP), are more likely to experience pro-longed symptoms and cognitive impairments after concussion (Su et al., 2014).

7.7. Blood-Brain Barrier Dysfunction

The BBB plays a critical role in maintaining brain homeostasis, but it becomes compromised following mTBI. Animal studies have shown that BBB dysfunction can persist for hours to days post-injury, with evidence of increased permeability and de-creased expression of junctional proteins (Yeung et al., 2008; Nag et al., 2009). Some studies suggest a biphasic re-sponse, where early BBB disruption is followed by delayed dysfunction, potentially contributing to prolonged neurological symptoms (Baldwin et al., 1996; Başkaya et al., 1997).

Human studies have also identified BBB disruption following concussion, with neuroimaging techniques revealing increased permeability in athletes exposed to sub-concussive impacts and mTBI (Raghupathi et al., 2002; Korn et al., 2005). The extent and duration of BBB dysfunction in humans remain areas of active research, with current findings suggesting a variable recovery timeline.

7.8. Cell Death

While cell death is less pronounced in mild TBI compared to severe TBI, animal models have demonstrated limited neuronal apoptosis following mTBI, particularly in vulnerable areas like the cortex and thalamus (Su et al., 2014). Human studies using advanced neuroimaging techniques have shown region-specific brain volume loss following concussion, particularly in the

hippocampus and limbic system (Mavroudis et al., 2022). These findings suggest that even mild brain injuries can lead to long-term structural changes, which may correlate with cognitive and psychiatric outcomes.

8. How a Concussion can disrupt Markov Blankets in the brain

A concussion disrupts the normal functioning of the brain through several key bi-ological mechanisms, each of which has the potential to interfere with the stability and function of Markov blankets. The primary neurometabolic cascade following a concus-sion includes ionic flux, neurotransmitter release, mitochondrial dysfunction, energy crises, neurovascular changes, axonal injury, and neuroinflammation. These processes contribute to the breakdown of the finely tuned balance between internal and external states, undermining the ability of Markov blankets to maintain conditional independ-ence and functional coherence.

8.1. Ionic Flux and Neurotransmitter Release

One of the immediate effects of a concussion is the disturbance of cellular homeo-stasis due to ionic flux and neurotransmitter release. Mechanical forces transmitted to the brain cause "mechanoporation," disrupting the plasmalemmal membrane and re-sulting in the outflow of potassium and depolarization of neurons (Steenerson et al., 2017). This wide-spread depolarization triggers a release of excitatory neurotransmitters like glutamate, which binds to NMDA receptors, perpetuating a feedback loop of depolarization and hyperexcitability (Mc Fie et al., 2018; Giza and Hovda, 2001).

In terms of Markov blankets, this ionic flux and neurotransmitter release disrupts the normal flow of information between sensory and active states. The feedback loop of depolarization and hyperexcitability increases noise in the system, making it difficult for the brain to accurately predict and interpret sensory inputs. This noise can distort the internal models that the brain uses to represent the external world, leading to cognitive impairments. The disruption of this balance also affects memory, as the processes of encoding, consolidation, and retrieval rely on the accurate prediction and integration of sensory inputs.

8.2. Calcium Accumulation and Mitochondrial Dysfunction

Following the initial ionic flux, calcium accumulates within neurons, leading to mitochondrial impairment (Cheng et al., 2012; Barkhoudarian et al., 2011). This impairs the brain's ability to meet the in-creased metabolic demands necessary for restoring ionic homeostasis. The resulting energy crisis, characterized by hyperglycolysis followed by glucose hypometabolism, further exacerbates the brain's vulnerability (Kawamata et al., 1995; Kalimo et al., 1981).

Mitochondrial dysfunction disrupts the energetic balance needed to sustain the activity of neurons, particularly in regions critical for cognitive processing, such as the hippocampus and prefrontal cortex. Markov blankets at the cellular level rely on effi-cient metabolic processes to maintain the separation between internal and external states. When energy supply is insufficient, the active states (which drive interactions with the external environment) become less reliable, leading to deficits in attention, working memory, and executive function. The breakdown of energy supply mecha-nisms compromises the ability of neurons to engage in synaptic plasticity, which is es-sential for memory formation and cognitive flexibility.

8.3. Blood Flow and Neurovascular Changes

Concussion also affects cerebral blood flow (CBF), with alterations in both global and regional perfusion observed following mTBI (Choe et al., 2012). These changes can be attributed to autoregulatory and vasoreactive disturbances, which compromise the brain's ability to maintain stable blood flow in response to metabolic demands. Decreases in CBF have been observed in

regions associated with emotion regulation and autonomic con-trol, such as the insula and cingulate cortex, further complicating cognitive and emo-tional regulation post-injury (Thibeault et al., 2018).

The stability of Markov blankets depends on the brain's ability to efficiently match metabolic demands with blood supply. When blood flow is compromised, the ability of neurons to process information is impaired, leading to cognitive slowing and reduced capacity for memory consolidation. The hypometabolic phase that follows a concus-sion increases the brain's vulnerability to subsequent injuries during the "window of vulnerability" (Prins et al., 2013; DeFord et al., 2022), highlighting the importance of stable neurovascular function in maintaining Markov blankets. Without adequate blood flow, the separation between internal and external states becomes blurred, leading to disruptions in both cognitive function and memory retention.

8.4. Axonal Injury and Synaptic Dysfunction

Concussions induce mechanical forces that lead to diffuse axonal injury (DAI) by stretching and shearing axons. This disrupts axonal transport, leading to the accumulation of beta-amyloid precursor protein (b-APP) and other neurotoxic proteins (Johnson et al., 2013). Axonal injury impairs the transmission of electrical signals between neurons, which is critical for maintaining communication across neural circuits.

Axonal integrity is essential for the proper functioning of Markov blankets at the level of neural circuits. When axons are damaged, the ability of sensory states to influ-ence internal states becomes compromised, as the transmission of information between brain regions becomes less efficient. This is particularly relevant in regions involved in memory, such as the hippocampus, where axonal injury can disrupt the flow of infor-mation necessary for the consolidation of episodic memories. The impairment of axon-al transport also affects working memory, as the prefrontal cortex relies on the timely transmission of information to guide behavior based on past experiences.

8.5. Neuroinflammation and Blood-Brain Barrier Dysfunction

Neuroinflammation is a hallmark of concussion, characterized by the activation of microglia and the release of inflammatory cytokines like interleukin 1β (IL-1B) and interleukin 6 (IL-6) (Rathbone et. al, 2015), (Reeves, 2005). This inflammatory response can perpetuate cellular dam-age beyond the initial injury site, contributing to ongoing cognitive impairments. Ad-ditionally, the breakdown of the blood-brain barrier (BBB) allows peripheral immune cells to infiltrate the brain, further exacerbating neuroinflammation and disrupting homeostasis (Su et al., 2014).

The presence of neuroinflammation disrupts the normal functioning of Markov blankets by increasing the permeability of the brain to external factors, such as im-mune cells and inflammatory signals. This leads to increased variability in sensory in-puts, making it difficult for the brain to maintain accurate internal models. The break-down of the BBB also allows toxic substances to enter the brain, increasing the likeli-hood of cognitive decline. The disruption of Markov blankets in this context impairs memory consolidation, as inflammation interferes with synaptic plasticity and the ability of neurons to form stable connections necessary for long-term memory.

8.6. Impaired Synaptic Plasticity

Synaptic plasticity, the brain's ability to strengthen or weaken connections be-tween neurons based on experience, is essential for learning and memory. Concussion disrupts this process by altering the function of NMDA receptors and GABA-ergic in-terneurons, which are crucial for maintaining excitatory-inhibitory balance in the brain (Raghupathi et al., 2002).. These changes impair long-term potentiation (LTP), a key mechanism for memory consolidation, particularly in the hippocampus and prefrontal cortex (Kalimo et al, 1981).

Markov blankets rely on synaptic plasticity to dynamically update the brain's in-ternal models of the external environment. When plasticity is impaired, the brain be-comes less flexible in its ability to integrate new information, leading to deficits in both short-term and long-term memory. Impaired LTP disrupts the formation of new mem-ories, while impaired long-term depression (LTD) affects

the brain's ability to eliminate outdated or irrelevant information. These disruptions lead to cognitive rigidity, mak-ing it difficult for individuals with concussion to adapt to new situations or recall in-formation accurately.

9. Evidence from fMRI studies

9.1. Disruption of the DMN in mTBI Patients

Functional Magnetic Resonance Imaging (fMRI) can detect alterations in brain activity by measuring changes in blood flow, which correlate with neuronal activation. By comparing brain network activity in patients with mild traumatic brain injury (mTBI) to healthy controls, fMRI can identify dysfunctional areas in cognitive networks that align with the disruptions predicted by your model. It can be used to track how mTBI affects functional connectivity, particularly in regions responsible for attention, memory, and executive function. Findings from studies utilizing resting-state fMRI show that mTBI patients exhibit significant disruption within the DMN. Specifically, there is a decrease in connectivity in the posterior regions and an increase in connectivity in the frontal regions (Ken et al., 2022). This pattern suggests a disruption in the normal functional equilibrium between DMN regions, likely reflecting the disturbance of information flow across Markov blankets in the brain.

These disruptions have been shown to correlate with specific cognitive deficits in mTBI patients:

- Reduced connectivity in the posterior DMN is associated with memory and cognitive flexibility impairments, both of which rely on the brain’s ability to effectively encode and retrieve information (Ken et al., 2022).
- Increased frontal connectivity has been correlated with posttraumatic symptoms such as depression, anxiety, and fatigue (Ken et al., 2022).

These opposing connectivity changes within the DMN can be viewed as reflecting a dynamic but maladaptive response to the disruption of Markov blankets. The DMN normally supports internal cognitive processes during rest, but its disruption may force other regions to compensate for the loss of function, leading to cognitive deficits.

9.2. Methods: Simulation of Markov Blankets and Disruption in Post-Concussion Syndrome

The aim of this simulation was to model the effect of mild traumatic brain injury (mTBI) on the brain’s cognitive and sensory processing, using the Markov blanket framework. The Markov blanket system is designed to simulate how the brain's internal (neural processes) and external states (environmental stimuli) interact via sensory and active states. By introducing noise and perturbations to reflect mTBI-related disruptions, we aimed to observe how these changes affect the brain's ability to maintain conditional independence, predictive coding, and cognitive function.

10. Model Design and Structure

10.1. Defining the Markov Blanket

The system was structured based on the standard Markov blanket configuration, consisting of:

- Internal States (μ): Representing neural processes such as cognitive func-tions (e.g., memory, reasoning).
- External States (η): Representing external stimuli or environmental factors affecting the brain.
- Sensory States (s): Mediating the influence of external states on internal states by processing sensory inputs.

- Active States (a): Mediating the influence of internal states on external states, reflecting behavioral outputs and responses.

In a healthy brain, this structure ensures that internal and external states remain conditionally independent, with sensory and active states facilitating communication and maintaining system stability.

10.2. Stochastic Differential Equations (SDEs)

The dynamics of the system were modeled using stochastic differential equations (SDEs), which describe the evolution of internal, external, sensory, and active states over time. The equations used for the simulation were as follows (1):

$$\dot{\mu} = f_{\mu}(\mu, s, a) + \sigma_{\mu} W(t)$$

$$\dot{s} = f_{s}(\eta, s) + \sigma_{s} W(t)$$

$$\dot{a} = f_{a}(\mu, s) + \sigma_{a} W(t)$$

$$\dot{\eta} = f_{\eta}(\eta, s, a) + \sigma_{\eta} W(t) \quad (1)$$

Where:

- μ represents **internal states,** referring to the cognitive processes occurring within an individual, such as thoughts, emotions, and decision-making, influencing behavior and responses to external stimuli. (e.g., cognitive processes),
- η represents **external states,** encompassing environmental stimuli that can impact an individual's internal cognitive processes, including sensory inputs such as sights, sounds, and other environmental factors that interact with and influence an individual's cognitive and emotional responses (e.g., environmental stimuli),
- s represents **sensory states,** mediating the influence of external stimuli on internal cognitive processes, playing a crucial role in how we perceive the environment and respond to it. For example, sensory states could include visual or auditory processing that directly impacts attention and memory tasks (mediating external influence on internal states),
- a represents **active states** referring to the processes that mediate the influence of internal cognitive states on an individual's actions, includeing how thoughts, emotions, and intentions lead to behavioral outcomes (mediating the influence of internal states on external actions),
- W(t) represents the **Wiener process**, a mathematical representation of random motion, often used to model stochastic processes in various fields, including physics and finance and in the context of cognitive modeling, it introduces stochastic noise to represent the inherent variability in cognitive processes over time.
- σ represents **noise terms specific to each state** and represent the variability or uncertainty within that state, occuring can account for discrepancies due to external influences or internal cognitive fluctuations.

This baseline model simulates a stable system where Markov blankets are intact, and the brain can effectively process sensory information and respond to external stimuli. The internal and external states evolve independently, mediated by sensory and active states, which ensures efficient prediction and response processes in the brain.

10.3. Introducing mTBI Disruptions

To simulate the effects of mTBI, we modified the baseline system by introducing additional noise and reducing the interaction strength between internal, sensory, ac-tive, and external states.

This disruption was modeled as follows (2):

$$\dot{\mu}=f_\mu(\mu,s,a)+\sigma_\mu W(t)+\Delta\mu \quad \dot{\mu}=f_\mu(\mu,s,a)+\sigma_\mu W(t)+\Delta\mu \quad \dot{s}=f_s(\eta,s)+\sigma_s W(t)+\Delta s \quad \dot{s}=f_s(\eta,s)+\sigma_s W(t)+\Delta s \quad \dot{a}=f_a(\mu,s)+\sigma_a W(t)+\Delta a \quad \dot{a}=f_a(\mu,s)+\sigma_a W(t)+\Delta a \quad \dot{\eta}=f_\eta(\eta,s,a)+\sigma_\eta W(t)+\Delta\eta \quad \dot{\eta}=f_\eta(\eta,s,a)+\sigma_\eta W(t)+\Delta\eta \quad (2)$$

where:

- $\Delta\mu$, Δs, Δa, $\Delta\eta$ represent additional noise introduced by mTBI, mimicking the effects of ionic imbalances, neurotransmitter dysregulation, and synaptic damage.

These disruptions reflect the common physiological and neurochemical changes observed after mTBI, including glutamate toxicity, impaired synaptic transmission, and decreased cerebral blood flow (CBF).

11. Simulation of mTBI Disruption

The system was simulated twice:

1. Baseline Condition: A stable system was modeled without injury, where the dynam-ics evolve according to normal brain function, and the Markov blankets remain intact.

2.Post-mTBI Condition: Disruptions were introduced, reflecting the neural and bio-chemical changes caused by mTBI. This led to impaired sensory processing, delayed motor responses, and increased internal noise, simulating cognitive deficits and motor dysfunction seen in post-concussion syndrome (PCS).

Key disruptions included:

- Increased Noise in Sensory States (s): Representing neurotransmitter dysregulation and impaired sensory processing (e.g., glutamate release).
- Reduced Connectivity Between Internal (μ) and Active States (a): Simulat-ing impaired synaptic transmission and slower motor response times.
- Delayed Synchronization Between States: Reflecting the overall cognitive slowdown and loss of predictive coding efficiency.

12. Results

12.1. Pre-mTBI Simulation:

- In the baseline simulation, the system exhibited stable, well-regulated dis-tributions for each state. Sensory (s) and active (a) states effectively mediated the in-teraction between internal (μ) and external (η) states, maintaining system stability and coherence.
- Distributions of internal, sensory, and active states were concentrated, re-flecting efficient cognitive function and motor responses.
- The Markov blanket ensured smooth and error-free predictions and re-sponses to external stimuli.

12.2. Post-mTBI Simulation:

- After introducing mTBI-related disruptions, the system exhibited broader, less concentrated distributions of internal, sensory, and active states, reflecting in-creased noise and system instability.
- Sensory Processing Impairment: Sensory states (s) showed increased vari-ance, reflecting the post-mTBI disturbances in neurotransmitter regulation and im-paired sensory processing.
- Delayed Motor Response: Active states (a) exhibited delayed response to internal states (μ), simulating the impaired motor function and reaction time observed in PCS.
- Cognitive Instability: Internal states (μ) became more dispersed, indicating impaired cognitive processing, memory deficits, and difficulties with predictive cod-ing.

- Loss of Synchronization: The interaction between states was delayed, re-flecting the brain's impaired ability to integrate sensory inputs and motor outputs ef-fectively.

The simulation effectively demonstrated the impact of mTBI on the brain's ability to maintain conditional independence and the functioning of Markov blankets. In-creased noise and decreased connectivity led to cognitive and sensory processing defi-cits that align with the symptoms of post-concussion syndrome, such as memory im-pairment, slower reaction times, and sensory overload.

13. Distribution of Active State (a)

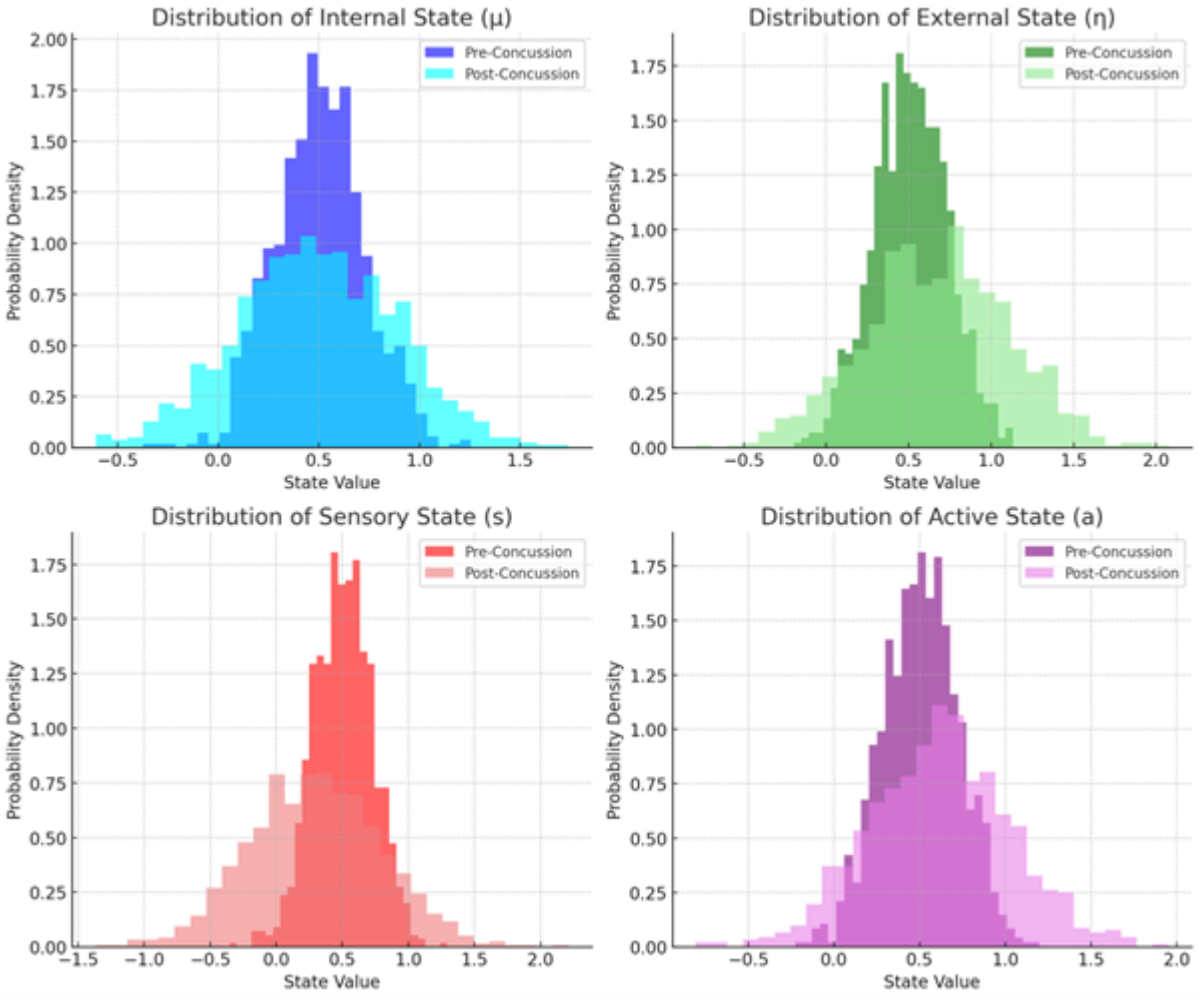

Figure 1. The visualizations above represent the probability distributions of internal (μ), external (η), sensory (s), and active (a) states before and after a concussion (mTBI). These distributions illustrate how a concussion can alter the normal functioning of the brain by disrupting the conditional dependencies between these states:

1. Internal State (μ): Pre-concussion (blue) shows a tighter, well-regulated distribution, while post-concussion (cyan) shows a broader, more dispersed distribution, reflecting the increased noise and dysregulation of internal processes after the injury.
2. External State (η): The pre-concussion state (green) has a stable, narrow distribution, while the post-concussion distribution (light green) is wider, indicating the impact of neurovascular and metabolic changes on how external stimuli are processed after the injury.
3. Sensory State (s): The pre-concussion sensory state (red) shows a tight, controlled distribution, while the post-concussion sensory state (light red) has a higher variance, representing disruptions in sensory processing, such as neurotransmitter dysregulation and impaired sensory input processing.

4. Active State (a): The pre-concussion active state (purple) shows a concentrated distribution, whereas the post-concussion active state (light purple) exhibits a broader distribution, indicating the delayed or disrupted responses in motor outputs and other active processes after the injury.

These shifts in the distributions reflect the physiological and neurochemical disruptions that occur after a concussion, such as altered synaptic connectivity, neurotransmitter imbalances, and impaired communication between the brain and external stimuli.

Incorporating this approach into research and clinical practice can help in understanding how concussions disrupt the brain's predictive coding mechanisms, leading to the breakdown of Markov blankets and contributing to post-concussion syndrome symptoms such as cognitive deficits, memory impairment, and sensory dysfunction.

14. Comparative Analysis of the Markov Blanket Model in Understanding Cognitive Dysfunction Post-mTBI

The Markov blanket model provides a unique lens through which to examine cognitive dysfunction following mild traumatic brain injury (mTBI). To enhance the relevance and depth of this analysis, it is essential to compare the Markov blanket approach with several established theoretical frameworks and empirical studies.

14.1. Predictive Coding Models

The framework of predictive coding, as articulated by Friston (2010) and Clark (2013) posits that the brain continuously updates its predictions based on sensory input. This model emphasizes the significance of prediction errors in shaping cognitive processes. By comparing the Markov blanket model with predictive coding, we can explore how disruptions in internal states (cognitive processes) may affect an individual's ability to make predictions and adapt to environmental changes after mTBI. This comparison could reveal new insights into how cognitive dysfunction manifests in individuals recovering from injury.

14.2. Dynamic Causal Modeling (DCM)

Research on Dynamic Causal Modeling (DCM) by Friston et al. (2003) and Stephan et al. (2010) serves as a vital point of comparison. DCM focuses on the causal relationships between brain regions and their connectivity patterns. Examining the distinctions between the Markov blanket model and DCM can illuminate how each approach represents disruptions in brain connectivity. For instance, the Markov blanket model's emphasis on the interaction between internal and external states can complement the causal inferences drawn from DCM, enhancing our understanding of cognitive dysfunction in mTBI.

14.3. Neuroplasticity Models

Models of neuroplasticity, such as those by Zotey et. al 2023 and Kerr et. al 2023 explore the brain's ability to reorganize itself following injury. Comparing these neuroplasticity frameworks with the Markov blanket model can provide a richer context for understanding recovery processes. The Markov blanket model may elucidate how cognitive states can influence neuroplastic changes, thereby informing rehabilitation strategies for individuals with mTBI.

14.4. Empirical Evidence on Neurovascular Changes

Studies by Giza & Hovda (2014) and Churchill et al. (2017) provide empirical data on neurovascular alterations following mTBI. Integrating these findings into the discussion can enhance the theoretical framework of the Markov blanket model. By correlating theoretical insights

with empirical evidence regarding changes in brain connectivity and vascular responses, a more comprehensive understanding of cognitive deficits following mTBI can be achieved.

Incorporating these comparisons not only strengthens the theoretical foundation of the Markov blanket model but also situates it within a broader academic context. Future research should explore these intersections to enhance our understanding of cognitive dysfunction and recovery strategies in individuals with mTBI.

15. Discussion

A concussion disrupts the Markov blanket by introducing disturbances in both the sensory and active states. The sensory states fail to effectively mediate between the external and internal environments, leading to poor perception and disorganized cognitive function. Active states struggle to convert internal signals into appropriate behavioral responses, resulting in delayed or abnormal actions. The system as a whole becomes unstable, unable to maintain the coherence needed for normal cognitive and motor function, mirroring the symptoms of concussion.

This disruption is caused by factors such as ion imbalances (e.g., increased potassium and calcium), neurotransmitter release (e.g., excess glutamate), axonal injury, and changes in blood flow, which together impair the brain's ability to maintain conditional independence and functional coherence . The Markov blanket structure, which relies on these precise interactions, becomes compromised, leading to the cognitive, sensory, and motor dysfunction observed in concussed individuals.

Some ractical implications of this model for clinicians or researchers working on mTBI:

1. Enhanced Diagnostic Tools:

The theoretical framework can aid in developing diagnostic tools that leverage neuroimaging data (e.g., fMRI, DTI) to identify disruptions in brain networks associated with mTBI. By utilizing the concept of Markov blankets, clinicians could better isolate variables influencing cognitive outcomes, thus refining diagnostic criteria for mTBI-related cognitive dysfunction .

2. Personalized Treatment Strategies:

Understanding the internal and external states defined by the model can facilitate tailored rehabilitation programs. Clinicians could design interventions based on specific cognitive profiles and environmental influences, improving treatment efficacy. For instance, interventions could target particular cognitive processes identified as impaired through the framework .

3. Predictive Modeling of Outcomes:

The integration of Markov blankets allows for the creation of predictive models that estimate the likelihood of cognitive recovery based on initial assessments. This can help clinicians anticipate long-term outcomes and adjust treatment plans proactively .

4. Research into Mechanisms of Recovery:

For researchers, this model offers a structured approach to investigate the mechanisms underlying cognitive recovery post-mTBI. By analyzing how different states interact, researchers can identify key factors that facilitate or hinder recovery, contributing to the development of more effective rehabilitation protocols .

Disruption of Markov Blankets Post-Concussion

Under the predictive coding framework, the brain functions to minimize prediction errors, or free energy, by continuously updating its internal models based on incoming sensory data. The Markov blanket structure plays a key role in this, ensuring a smooth flow of information between internal and external states via sensory and active states.

In MTBI, findings from fMRI studies have shown significant disruption in DMN connectivity. Specifically, there is a reduction in functional connectivity within the posterior cingulate cortex (PCC) and parietal regions, with an associated increase in medial prefrontal cortex (MPFC) activity . This disruption aligns with what we would expect if the Markov blanket was no longer intact. The internal states (neural processes, for example) become less insulated from the

external environment due to the breakdown in sensory and active state mediation, leading to prediction errors and increased free energy.

Predictive Coding and Increased Free Energy

Predictive coding posits that the brain generates internal models of the world to predict incoming sensory data. When the predictions match the actual sensory input, prediction errors are minimized, and the system operates efficiently. However, when a concussion disrupts the brain's ability to process information—due to damage in the sensory and active states—prediction errors become frequent, and the free energy in the system rises.

In the DMN, the observed hyperconnectivity in the MPFC may represent a compensatory mechanism to deal with the increased free energy following the injury. The brain tries to restore the balance by hyperactivating certain regions to compensate for reduced connectivity elsewhere (e.g., in the PCC and parietal regions), but this comes at a cognitive cost, as seen in post-concussive symptoms like memory deficits, depression, and anxiety.

fMRI Studies and Free Energy

fMRI studies have consistently shown that patients with MTBI exhibit reduced posterior connectivity in the DMN, which correlates with cognitive dysfunction (e.g., decreased cognitive flexibility) . The increased functional connectivity in the MPFC is negatively correlated with symptoms of depression and anxiety, suggesting that this region might be overcompensating for the loss of function elsewhere in the network . This imbalance between different parts of the DMN could reflect the brain's attempt to minimize the prediction errors caused by disrupted Markov blankets.

Moreover, the changes in functional connectivity seen in fMRI studies align with the idea that a concussion leads to a persistent state of increased free energy in the brain. The DMN, which is normally responsible for resting-state cognitive processes, becomes less efficient at managing the flow of information between internal and external states, leading to symptoms associated with cognitive overload, such as mental fatigue and reduced attentional capacity.

Future Directions and Research

The exploration of Markov blankets in the brain, particularly in the context of concussion, opens exciting new avenues for future research. A deeper understanding of how the brain's connectivity and processing systems are disrupted by concussions can help improve diagnostic tools, treatment approaches, and recovery strategies. Some key areas of future research include:

Modeling Concussions with Markov Blankets: Research should focus on further refining models of brain dynamics using the Markov blanket framework to simulate the effects of concussions. These simulations can better predict how different regions of the brain are impacted, leading to a more individualized understanding of cognitive and motor impairments after traumatic brain injuries (TBI). By incorporating real-world data from neuroimaging and electrophysiological studies, these models can be calibrated to better reflect specific cases of concussion.

Predictive Coding and Active Inference in Concussion Recovery: Future research could explore how disruptions to predictive coding and active inference—both of which are closely tied to the Markov blanket framework—impede cognitive recovery. Understanding how concussions disrupt the brain's ability to predict and process external stimuli could lead to new therapeutic strategies. For example, therapies aimed at restoring the brain's capacity for accurate prediction and sensory processing may improve cognitive function post-injury.

Advanced Neuroimaging Techniques: Cutting-edge imaging technologies, such as functional MRI (fMRI) and diffusion tensor imaging (DTI), are essential in studying how concussions affect the brain's structural and functional networks. DTI focuses on white matter integrity by measuring the diffusion of water molecules along neural pathways. This technique is valuable for identifying

microstructural damage to white matter tracts that often occur in mTBI, helping to visualize disconnections between brain regions. Changes in white matter tracts could reflect the external states and internal disruptions modeled in your work. Research that combines these imaging techniques with Markov blanket models could yield new insights into how different regions of the brain are affected and how these changes evolve during recovery. Additionally, longitudinal studies tracking brain recovery using these tools could help establish timelines for healing and identify the factors that promote faster or more complete recovery.

Biomarker Identification: Identifying biomarkers associated with concussion-induced disruptions to Markov blankets could greatly improve diagnosis and monitoring. Biomarkers such as altered neurotransmitter levels, metabolic changes, and specific patterns of brain connectivity (e.g., disruptions in the default mode network) can be incorporated into clinical assessments to create more objective measures of concussion severity.

Implications for Recovery and Rehabilitation

Neuroplasticity and Targeted Therapies: The brain's inherent neuroplasticity allows for potential recovery of disrupted Markov blankets following a concussion. Rehabilitation programs designed to promote neuroplasticity—such as cognitive training, physical exercise, and neurofeedback—could be tailored to strengthen weakened connections between sensory, active, internal, and external states. Research suggests that environmental enrichment and cognitive engagement can enhance recovery by encouraging neural reorganization, particularly in younger patients.

Early Intervention and Monitoring: Early identification of concussion-related disruptions to sensory and active states could guide interventions aimed at preventing further damage and accelerating recovery. Clinicians may use neuroimaging and cognitive assessments to monitor brain activity in real-time and detect abnormal patterns. Understanding how concussions affect Markov blankets can help clinicians implement personalized interventions at early stages, potentially reducing the risk of long-term cognitive decline.

Cognitive and Sensory Rehabilitation: Cognitive impairments following concussions, such as memory loss and attention deficits, are linked to disruptions in sensory and active states. Rehabilitation strategies that target specific deficits in sensory processing, such as vision or auditory therapies, can improve brain function by re-establishing the disrupted connections between external stimuli and internal processing.

Physical and Occupational Therapy: Motor impairments, often seen after concussions, stem from disruptions to active states. Physical therapy programs aimed at improving balance, coordination, and motor function can be enhanced by integrating Markov blanket principles. Training that specifically targets the restoration of feedback loops between motor actions (active states) and environmental feedback (external states) could improve physical recovery. This approach would involve re-establishing the connections that enable the brain to control movements effectively in response to environmental stimuli.

Addressing Long-Term Effects: Post-concussion syndrome (PCS) is a condition where symptoms persist long after the initial injury. Understanding how the long-term disruption of Markov blankets contributes to ongoing cognitive and emotional symptoms could guide the development of better treatments. Developing therapies that specifically target these disrupted mechanisms could offer relief for those with prolonged recovery times.

Clinical Importance and Meaning

Understanding Mechanisms of Brain Injury: The framework of Markov blankets provides a deeper understanding of how concussions affect brain function. By focusing on how the brain's internal and external states are disrupted, clinicians can gain a more nuanced understanding of the cognitive, sensory, and motor impairments following concussions. This understanding allows for a

more targeted approach to treatment, with therapies designed to restore the brain's predictive and sensory-processing capabilities.

Improved Diagnosis and Treatment Planning: The clinical relevance of this framework lies in its potential to enhance the diagnostic process. Current diagnostic tools often rely on subjective symptom reporting, which can lead to inconsistent or incomplete assessments. By integrating insights from Markov blanket models with neuroimaging and biomarker data, clinicians could develop more objective diagnostic criteria for concussions, leading to better treatment planning and monitoring.

Prevention of Secondary Injuries: The vulnerability of the brain following a concussion—such as during the "energy crisis" and periods of glucose hypometabolism—can be better understood through the lens of disrupted Markov blankets. Clinicians can use this knowledge to implement protective strategies to avoid secondary injuries. For instance, activity modification and proper recovery periods can help minimize the risk of further damage to the disrupted internal and external state interactions.

Personalized Medicine and Long-Term Care: With greater understanding of how concussions affect different individuals based on their specific brain networks and Markov blanket disruptions, personalized medicine approaches can be developed. This could involve tailored rehabilitation programs, pharmacological interventions targeting specific neurotransmitter imbalances, or neurofeedback techniques designed to restore disrupted feedback loops.

16. Conclusion

Understanding how concussions disrupt Markov blanket systems provides a comprehensive framework for addressing the cognitive, sensory, and motor impairments that follow such injuries. By modeling the interactions between internal, external, sensory, and active states, researchers and clinicians can gain new insights into how the brain recovers—or fails to recover—after concussions. The clinical implications are profound, as this approach can inform diagnostic tools, individualized treatment plans, and long-term care strategies aimed at improving outcomes for those suffering from concussions.

Concussion, specifically mild traumatic brain injury (MTBI), affects the brain’s default mode network (DMN) and the Markov blanket structure, impacting memory and cognitive function. In a healthy brain, Markov blankets help maintain conditional independence between internal states (e.g., neural processes), external states (e.g., environmental stimuli), and their intermediaries—sensory and active states. However, in the case of a concussion, the dynamics of this separation are disrupted, which could lead to a breakdown of predictive coding and an increase in free energy in the system.

The disruptions in brain networks modeled in the context of mTBI, particularly within the default mode network (DMN), can be detected through advanced neuroimaging techniques such as functional MRI (fMRI) and diffusion tensor imaging (DTI). Studies using fMRI have shown that mTBI leads to significant changes in brain connectivity. For example, a reduction in posterior connectivity, such as within the posterior cingulate cortex (PCC), and increased connectivity in the medial prefrontal cortex (MPFC), are common indicators of cognitive dysfunction. These alterations suggest that the brain is compensating for the loss of normal function by hyperactivating certain regions, which can be linked to symptoms such as memory deficits, depression, and anxiety.

Additionally, the Markov blanket model can inform diagnostic tools and rehabilitation strategies. By simulating the disruptions caused by mTBI, clinicians can better understand how the brain's predictive coding and sensory processing are affected. This insight can lead to more objective diagnostic criteria by integrating neuroimaging and biomarkers with predictive modeling. Rehabilitation strategies might include targeted cognitive therapies or neurofeedback techniques aimed at restoring disrupted feedback loops between internal and external states, aiding in cognitive recovery.

In conclusion, applying the Markov blanket model in clinical settings could significantly enhance the diagnosis and treatment of cognitive dysfunction following mTBI. Specifically, this model could be used to monitor disruptions in neural networks and cognitive processes, providing a deeper understanding of how the brain responds to injury. For instance, functional neuroimaging techniques such as fMRI and EEG could be integrated within this framework to assess changes in brain connectivity, particularly in networks responsible for attention and memory. These data could facilitate accurate diagnosis of cognitive impairments and support the development of personalized rehabilitation programs tailored to the severity of the injury. Additionally, the model could inform therapeutic interventions, such as cognitive training or neurofeedback, to promote neuroplasticity and accelerate recovery

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