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Heuristics and biases in medical decision-making under uncertainty: the case of neuropronostication for consciousness disorders

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ABSTRACT

Neuropronostication for consciousness disorders can be very complex and prone to high uncertainty. Despite notable advancements in the development of dedicated scales and physiological markers using innovative paradigms, these technical progressions are often overshadowed by factors intrinsic to the medical environment.

Beyond the scarcity of objective data guiding medical decisions, factors like time pressure, fatigue, multitasking, and emotional load can drive clinicians to rely more on heuristic-based clinical reasoning. Such an approach, albeit beneficial under certain circumstances, may lead to systematic error judgments and impair medical decisions, especially in complex and uncertain environments.

After a brief review of the main theoretical frameworks, this paper explores the influence of clinicians' cognitive biases on clinical reasoning and decision-making in the challenging context of neuroprognostication for consciousness disorders. The discussion further revolves around developing and implementing various strategies designed to mitigate these biases and their impact, aiming to enhance the quality of care and the patient safety.

KEYWORDS

Heuristics, cognitive biases, human factors, clinicians, reasoning, decision-making, prognosis, diagnosis, behavioral science, metacognition.

1. Dive-in: the challenge of human factors, example of the neuropronostication of comatose patients

1.1. *The complexity of neuropronostication for consciousness disorders*

Many ongoing research works focus on developing innovative ways to probe consciousness in clinically unresponsive patients relying on new markers, improved scales and paradigms or recently developed tools to improve the quality of care provided in emergency departments and intensive care units (ICU). However, beyond current technical limitations, several factors inherent to these medical environments strengthen the complexity of neuropronostication in the ICU. Among them, a very high level of uncertainty regarding the evolution of the patient's condition and the absence of knowledge of the patient's preferences, for instance, add up to the scarcity of objective and measurable cues of consciousness. In addition to these practical constraints, human factors such as practitioners' experience, ethical and moral beliefs or staffs' collective dynamics can also influence clinical reasoning and decision-making processes during goals-of-care decisions.

In this perspective, several experimental studies recently highlighted the poor reliability and inter-individual inconsistency in forecasting the outcomes of brain-injured patients with disorders of consciousness across physicians. This is well illustrated by a recent online simulation exercise in which clinical and complementary data available within the first 24h for cases of severely injured patients were presented to 120 physicians from the neurological department of the Massachusetts General Hospital (neurocritical care, stroke or other subspecialties) [1]. Participants were asked to rank the five patients (2 with large hemi-spheric infarction; 1 with brainstem infarction, 1 with lobar hemorrhage, and 1 with hypoxic-ischemic encephalopathy) based on the provided data. Although the pooled predictions (wisdom of the crowd) reached a fair level of prediction quality (3% accurate prediction) at the group level, respondents showed important variability in their predictions, when compared to real patients' outcomes (ranging from 2% to 95% accuracy), without significant impact of experience (faculty vs trainees) nor subspecialty (neurocritical care/stroke vs other). An important variability was also found in another study done among 742 neurologists and neurosurgeons providing their predictions of 30-day mortality while facing different case-scenarios versions of patients with intracerebral hemorrhage with variations in several parameters (age, lesions location, and severity of neurologic deficits) [2]. In another study, 111 experts were asked to give their predictions of outcome (death and disability) regarding 5 case-scenarios of patients with a common presentation of an acute ischemic stroke [3]. In this last study, accuracy of predictions was

lower than 50% for all outcomes, and below 20% for the primary outcome (prediction regarding death or disability of discharge).

Physicians often have to make high-stakes clinical decisions, such as setting goals-of-care and establishing optimal treatment plans in dialogue with surrogate decision-makers (opinions of patients with disorders of consciousness being frequently inaccessible by definition) [4]. Neuropronostication predictions enlighten these decisions and predicted poor functional outcomes frequently leads to decision to withdraw life-sustaining therapy [5]. Hence, all (human) factors potentially impacting neuropronostication and causing low accuracy and high variability between doctors' predictions towards patients with consciousness disorders should be further explored and better understood to develop solutions to mitigate their negative impact on medical decisions, enhance the quality of provided care and improve patient safety [5].

1.2. *Among human factors: cognitive biases*

The scarcity of objective data to guide medical decisions, alongside contingent parameters such as time pressure, fatigue or emotional load can drive ED physicians, intensivists and neurologists to rely on mental shortcuts called heuristics for their clinical reasoning and decision-making. Error judgments can arise in such situations, while facing tremendous uncertainty [3,6]. In particular, several cognitive biases have already been suspected to influence physicians' apprehension of perceived devastating brain injuries [7] or in other contexts [8,9]. As such, while it can be an effective strategy for physicians to rely on their intuitive statistical understanding of their practice environment to make a prognosis, the availability heuristic can for instance bias and undermine the decision-making process. This phenomenon indeed describes humans' propensity to judge the likelihood of an event occurring based on ease of recall (greater "availability" in memory) rather than on actual probabilities, and can lead doctors to over- or underestimate the likelihood of a certain prognosis based on a recent experience with a similar case.

Not only such cognitive mechanisms can lead to a distorted perception of reality, but they could also in turn affect the reality itself. In neuroprognostication, inaccuracies can occur in two different ways: predicting a positive outcome and being incorrect that can result in severe disability (e.g., persistent VS or MCS). Conversely, forecasting a negative outcome and being mistaken often leads to death in a context of WLST. These two inaccuracies are asymmetric because while mistakes in wrong optimistic predictions are easy to identify, in the latter case, they are frequently undetectable. A tendency towards pessimistic prognosis could then be attributed to cognitive biases such as loss

aversion, substitution bias, confirmation and selection bias [7]. Finally, since WLST frequently prevents clinicians to assess the truth and realize that their predictions of poor outcomes were incorrect, this can also lead to a survivorship bias where physicians'

Medical data inform neuroprognosis that can be straightforward but is more frequently difficult with a high remaining uncertainty. Goal-of-care decisions integrate neuroprognosis alongside other dimensions such as systemic and individual factors. Caregivers'

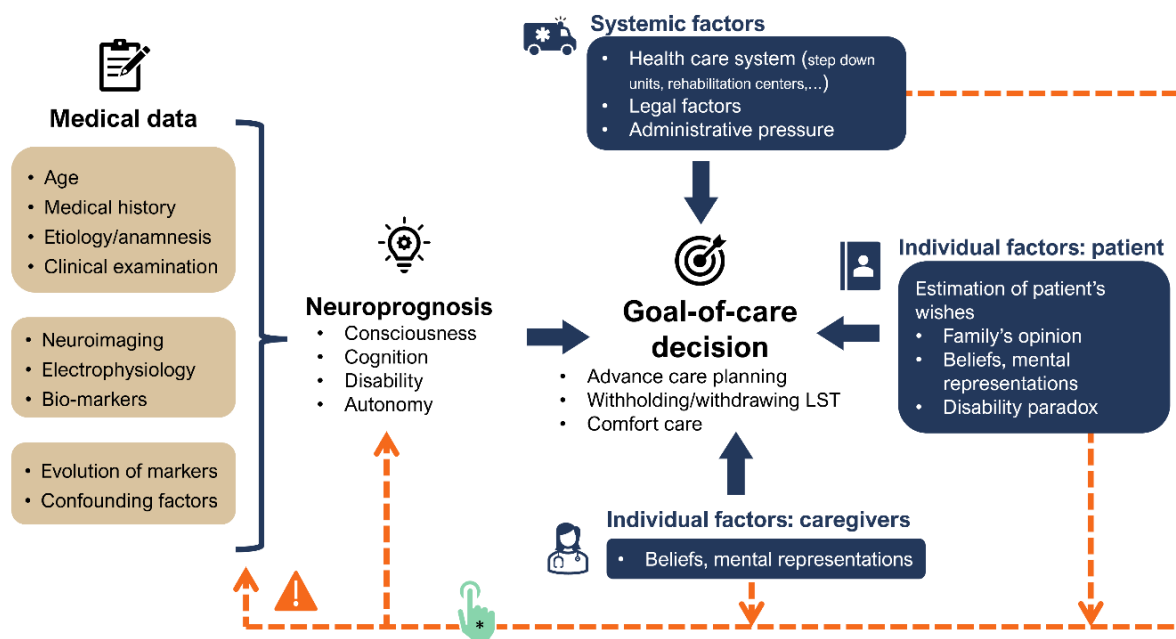


Figure 1. The complex scheme of decisions process in neuroprognostication of consciousness disorders.

experiences are skewed due to only observing and receiving feedback from a partial set of patients. This in turn can affect future decision-making, giving rise to the self-fulfilling prophecy phenomenon [10–12].

On the one hand, it could be considered as appropriate reasoning that systemic factors (such as health care system constraints) or patients, family and caregivers' beliefs and mental representations have an impact on medical plan and especially goal-of-care decisions (from full life support including invasive surgical procedure to exclusive comfort care). On the other hand, we would consider as inappropriate reasoning that such factors impact the interpretation of the medical data leading to revisiting the neuroprognosis in order comforts the goal-of-care decision (wishful thinking; read pathway in *Figure 1*).

Within this context of neuropronostication, a better understanding of cognitive mechanisms underlying medical decision under uncertainty, the identification of potentially systematic errors and the development of evidence-based strategies to mitigate if not to overcome medical mistakes thus constitutes priorities in order to enhance the quality of provided care and preserve patient safety.

beliefs and/or mental representations can impact goal-of-care decisions directly (appropriate reasoning) but also indirectly through a biased perception and (re)interpretation of medical data used for the neuroprognosis (orange arrows, e.g. wishful thinking, appropriate reasoning). The sign “*” represents potential behavioral science interventions that can mitigate the impacts of cognitive biases/ flawed reasoning.

2. Heuristics and cognitive biases in medicine: scientific background

2.1. General theoretical perspectives

2.1.1. The emergence of the theoretical interest in cognitive mechanisms. A growing interest in the study of the cognitive mechanisms underlying reasoning and decision-making arose during the 20th century. Several disciplines successively took up From the theory of expected utility proposed by mathematicians (von Neumann, Morgenstern), a strategic method aimed at making optimal decisions was developed, later completed by Bayesian statistics (Laplace, Bayes and Savage) and qualified as decision analysis (Raiffa, Howard). Decision analysis consists, after formulating the problem and listing the possible options, in studying

these options by determining for each one its expected utility, which represents the combination of its benefits and its probability of success. This strategy is particularly relevant in contexts that can be complex and risky but with low uncertainty, such as in industry, for example. This model was adopted by economists and led to the concept of *homo economicus*, a representation describing humans as rational agents in their decision-making. The *homo economicus* model depicts humans as theoretical fully rational decision-makers who know all the necessary information, objectively evaluate all options equally, and use computation to always make the optimal choice and maximize its own utility function. However, field observations of individuals' economic choices and, at a broader scale, of human decision-making in context of uncertainty revealed a myriad of behaviors violating the expected rational standards. Economic agents seem for instance to be influenced by the present bias, exhibiting a preference for a smaller immediate reward over a bigger delayed prize. Beyond economic choices, this phenomenon also largely affects health-related decisions, reducing individuals' and patients' compliance to health recommendations and guidelines [13] by the appeal of short-term pleasures (junk-food, smoking, sedentary lifestyle) at the expense of their health quality. The *homo economicus* theoretical perspective was thus empirically challenged by researchers in psychology who propose different alternatives views, such as the bounded rationality approach [14] that provides a better understanding of real, not always optimal, decision-making behaviors. This approach indeed takes into account human cognitive low-to-high order constraints such as the quantity and quality of neural information transmission and integration that are physiologically limited [15–19], limited attention, partial perception, biased reasoning or restricted memory [20–22].

2.1.2. Theoretical perspectives on heuristics and biases. Arising from the bounded rationality approach, several research programs developed alternative theoretical frameworks focusing on human reasoning and decision-making abilities.

- **Heuristics-and-bias: 2 speeds thinking systems.** The heuristics-and-bias approach was first developed by Kahneman and Tversky. In this model, the human brain is described as reasoning and deciding in many uncertain situations mainly relying on heuristics which are automatic mental shortcuts that help to judge, choose and act quickly or efficiently in many circumstances [22]. However, as heuristics rely on general knowledge arising from previous experiences rather than analytical thinking, the two authors suggest that their use can lead to systematic and predictable deviations in reasoning [22,23], called cognitive biases, that can lead to erroneous decisions. The heuristics-and-bias theory is

further illustrated by numerous experimental data identifying cognitive biases, collected in many different contexts.

Decades later, Kahneman integrated the outcome of the heuristic-and-bias research program within a simple model depicting two different reasoning and decision-making systems: a fast system 1 relying on intuitive and automatic heuristics prone to errors (called cognitive biases) and a second, slow and effortful system 2 relying on analytic thinking, hence more precise (Kahneman, 2011). Additional research works suggested the existence of an arbitration system relying on metacognitive abilities and inhibitory functions, eliciting the recruitment of system 1 or system 2 depending on the characteristics of the encountered situations [24–26]. The two-systems model received many criticisms, mostly questioning its compatibility with the much more complex reality and highlighting the lack of empirical data support [27].

- **Simple heuristics: ecological rationality.** In contrast to this view focusing on error-prone cognitive mechanisms (system 1 and heuristics leading to numerous biases), and beyond the hypothesis that brain has a preference for efficiency over accuracy [28], the perspective of ecological rationality later proposed by Gigerenzer and colleagues suggests that heuristics constitute an efficient and adaptive toolbox of strategies to make relevant decisions in most of the situations we encounter in our daily lives (*homo heuristicus*), especially under uncertainty [29]. As opposed to risk, uncertainty is characterized by an impossibility to predict all possible outcomes and consequences of a situation/decision, or the associated probability for each outcome to happen. Besides very specific controlled contexts such as lotteries, gambling and chest games, the complex world we live in is highly uncertain. According to the ecological rationality theory, the best way to react to such an unpredictable and unstable environment is to make decisions using rules-of-thumb or fast-and-frugal heuristics [30–33]. In this scope, simulation-based modelling for instance suggested that confirmation bias could be effective in information-seeking processes when combined with robust metacognitive abilities [34]. This framework, instead of questioning the rationality or optimality of human reasoning and decision-making processes (which highly vary depending on the context), rather challenges what is being set as the optimum in the heuristics-and-bias approach, and the relevance of the experimental paradigm used in subsequent field studies. Cognitive biases and the resulting errors are depicted as experimental artifacts arising from a mismatch between the context in which they are usually used (real-life situations) and the artificial environment in which they are being explored (laboratory settings) [35–38]. Although also criticized [39], this perspective aligns with a new computational approach to human rationality integrating the limits of available resources referred to as resource-rational analysis [40,41]. It also importantly sheds light on the meaning of

“uncertainty” in the context of real-life situations: the impossibility of anticipating all eventualities and/or their associated probability to happen, and therefore also the impossibility of identifying an optimal option while reasoning and deciding under uncertainty.

- **Evolutionary perspective.** Complementing the ecological rationality view, theoretical and data-based publications propose to explain cognitive biases by integrating them into an evolutionary perspective [42,43] and considering their emergence through the lens of the error management theory [44]. All dilemmas under uncertainty are modelled and analyzed in terms of the benefit/cost ratio associated with each possible type of choice, and in particular with possible errors (false negatives “false alarms” or false positive “misses”). If the relative costs of different types of error have been fundamentally asymmetrical over the course of human evolutionary history, then natural selection might have favored, “biased”, human behavior in a specific direction, that which minimizes the cost of error. This theory thus offers an explanation for many behaviors that appear irrational in nowadays’ environment, but would have emerged for evolutionary reasons and constitute adaptive biases for survival [42,43].

As an example, many cognitive biases can be categorized under “positive illusions,” which cause people to have an overly confident and unrealistic view of their own knowledge, abilities, and control over their environment and future [45]. This overconfidence can for instance lead individuals to underestimate the chances of experiencing health problems [46]. From an evolutionary standpoint, these positive illusions of unrealistic optimism about one’s ability to avoid health issues may be explained by error management theory [47]. This theory posits that behaviors that minimize the cost of error are more likely to be selected as adaptive: in this context, the greater cost would be failing to attempt to avoid preventable health problems, rather than trying to avoid inevitable ones. This perspective received common criticisms frequently addressed to the approaches based on evolutionary psychology [48–52], among which a lack of empirical evidence and the difficulty for its hypotheses to be falsified.

► **Practical implications: behavioral science applied “in the wild”.**

The study of reasoning and decision-making cognitive mechanisms through a psychological perspective thus led to the emergence of different theoretical approaches that in turn gave rise to recommendations to enhance individual and collective choices in various contexts. While a deeper understanding of these human abilities inspired new marketing and advertising strategies, a growing number of professional teams were created worldwide, hosted by governmental / academic institutions or non-profit organizations to apply behavioral science to public policies or

professional environments to promote better decisions among citizens or professionals. Applied behavioral science can take a myriad of different forms. The most popular, nudging, was developed [53] based on the heuristics-and-bias theory and consists of adapting the choice-architecture by taking into account citizens’ predictable biases to promote the most beneficial choice or behavior. On the other hand, boosting arose from the simple heuristics theory in line with the ecological rationality perspective [29,54], and aims at extending people’s decision-making competencies by providing adapted information or designing smart decision strategies [55,56]. Beyond the specificities of each approach, the application of behavioral science “in the wild” sheds light on the necessity to adopt evidence-based practices to elaborate user-centered interventions based on the available scientific literature to support decision-making and evaluate their impact with robust methodologies.

While debates are still ongoing between the different advanced theoretical currents and their practical implications, new attempts recently emerged to test existing theories and try to converge to a systemic and unified theory, based on biological features of the human brain [37] through imaging studies.

2.2. Application in the medical context

The medical context is inherently characterized by several environmental risk factors that can affect health professionals’ reasoning and decision-making: time pressure, emergency, stress [57,58], cognitive and emotional load [59–61], the need of multitasking, as well as sleep deprivation causing fatigue [62]. These conditions may potentiate individual and collective human factors such as limited attention, perception, reasoning and memory abilities or inter-individual differences and social dynamics, compromising the quality of low-to-high-stake decisions.

2.2.1. Appropriation of theories in medicine. In this context, the advanced theoretical perspectives aiming at better understanding reasoning and decision-making determinants and cognitive mechanisms and their associated practices to minimize errors due to human factors attracted practitioners’ attention. Several publications mainly rely on the heuristics-and-bias approach and focused on providing a comprehensive list of cognitive biases with their definition and an illustrative example of a medical situation prone to trigger the described phenomenon [63–69]. Others intend to bridge the gap by integrating theoretical frameworks within teaching recommendations and clinical practices. More specifically, the two-speed thinking systems model proposed by Kahneman mostly diffused in the medical environment and inspired reflective works on clinical reasoning [70], questioning the

respective relevance and combined use of systems 1 and 2 across situations [71,72], particularly in the scope of diagnosis performance improvement. In parallel, despite scarce citations [73] associated with an overrepresentation of Kahneman's approach, authors supporting the ecological rationality perspective specifically apply their theory to the medical context, testing its validity and advising doctors and medical students to develop and refine their heuristics in order to use them as smart strategies for medical decision-making [74–76]. This perspective is strengthened by subsequent studies suggesting that doctors' and caregivers' intuitions are often relevant and useful in the context of professional decision-making [77].

2.2.2. Spotting cognitive biases and their impact in the medical context. Apart from theoretical considerations, most efforts were so far devoted to tracking clinicians' biases and their impacts in the medical context, resulting in dozens of data-based or experimental studies (mainly relying on case-vignette scenarios) identifying and quantifying various cognitive phenomena [78–81]. As such, in a large retrospective study among ~10 000 US patients, the left-digit bias (the tendency to categorize continuous variables on the basis of the left-most numeric digit; this bias explains why items are more often priced at \$4.99 than \$5.00) was suggested to have a significant impact on doctors' decisions to perform (or not) a coronary-artery bypass graft surgery. This is a source of inequalities of treatments between patients aged just-below or just-above 80 years, with a subsequent and significant impact on mortality [82]. Similarly, in a retrospective analysis of surgical complications, cognitive biases were identified as root causes in 32.7% (241/736) of cases [83]. The presence of cognitive biases was correlated with a statistically significant increase in management errors and the occurrence of post-operative complications. Several publications further highlighted human factors and more specifically doctors' cognitive mechanisms and cognitive biases as the origin of a substantial proportion of occurring medical errors such as incorrect diagnosis [84–86].

The results of these investigations of cognitive biases “in the wild” are heterogeneous: they overall spotlight the wide range of their nature and prevalence in the clinical context. This variability might imply that each cognitive bias diagnosis is very specific to the explored situation, thus inherent to the study settings [78–81]. Beyond the current focus on cognitive biases, structural biases can emerge from practical settings and constraints, while other social biases can arise from the asymmetric interactions between health professionals and patients, for instance; these factors are also worth considering and exploring.

The marginal integration of the theories within studies conducted in the medical environment overall results in strong variability in nature of adopted experimental paradigms to spotlight cognitive biases affecting clinical decisions. These paradigms critically present a low-to-moderate robustness in terms of protocol, which increases the complexity of data interpretation and calls for precautions when drawing subsequent conclusions and recommendations for medical practice.

2.3. Insights towards mitigation solutions

Arising from global theoretical approaches aiming at describing and better understanding human reasoning and decision-making processes, new applied perspectives emerged for various topics of public policies. In the medical context, the observation of clinicians' cognitive biases lead to the conception and implementation of different types and scales of strategies to minimize their impact on the quality of provided care.

2.3.1. Sensitization and training of health professionals. Numerous mitigation interventions target clinical decision-makers themselves.

The simplest results from the ecological rationality perspective, and consists in advising clinicians, residents and medical students to rely on and further develop and refine their knowledge and heuristics through experience and feedback in order to use them as smart strategies for decision-making [74–76,87].

From a different perspective and in line with the heuristics-and-bias approach, some attempts to conceive debiasing strategies to target specific cognitive biases in precise situations proved to be at least partially effective [71,88,89]. However, such programs suffer from a low level of transferability from one situation to another, as highlighted in the literature about the teaching of critical thinking skills [90–94]. Furthermore, humans generally suffer from the propensity to be prone to identify and recognize cognitive biases in others' behavior while staying blind to their own [95,96]; this asymmetry might alter physicians' compliance to use such debiasing strategies.

To overcome the difficulty to elaborate universal debiasing solutions due to the variability in nature and prevalence of cognitive biases spotted in clinical situations across numerous studies, clinicians' sensitization to critical thinking and education of metacognition have received a growing amount of attention. Yet, and despite the risks represented by human factors for patient's safety, too few doctors are aware of the mechanisms and pitfalls behind human decision-making as most health professionals do not benefit from any training in critical thinking [97–100]. Thus, developing caregivers' reflective and metacognitive thinking

aptitude in the daily clinical practice through pedagogical contents could be an astute way to proactively empower and better prepare doctors for clinical decision-making [71–73,88,101–105], by enabling them to wisely arbitrate between different possible decision-making strategies (automatic vs. analytical systems) depending on many situational parameters (such as the level of experience, confidence, emergency, risk or uncertainty...) and to thoroughly monitor the quality of their reasoning processes and outcomes. The retrospective individual or collective analysis of adverse events in terms of cognitive causes of errors, referred to as cognitive autopsy, is an example of recommended reflective practice [98]. As such, and although the blind spot bias might alter this new skill towards their own practice [95,96], following a training 3-sessions curriculum about cognitive biases and associated diagnostic errors showed promising results by enabling 38 residents to spot cognitive biases in clinical scenarios [106]. Further research is needed to identify efficient methods to strengthen clinicians' metacognitive skills without interfering with performance or health professionals' well-being [73,107–109].

A last course of action in order to mitigate individual errors is to rely on the intrinsic characteristics of the human species' social cognition. Humans appear to be sensitive to their peers' actions and tend to follow the established social norm for reputational and survival purposes. This inclination is for instance used as leverage in the scope of applied behavioral science practices to address a wide variety of challenges. As such, social norms have been used in the medical context to tackle the issue of antibiotics overprescription, leading to the World threatening antibioresistance. This behavior can arise for different reasons: lack of information about the antibioresistance risks, habits, influence of patients' expectations... The intervention, tested both in the United Kingdom [110,111] and Australia¹, consisted of informing the highest antibiotics prescribers that they were prescribing more than the average of their colleagues, practicing in the same region. Doctors receiving this information adjusted their behavior to the norm and the interventions resulted in tens of thousands fewer prescribed antibiotics. Beyond social comparison, the quality of medical decisions could be improved by fostering collective reasoning and decision-making. According to the results of recent studies, outcomes arising from the wisdom of the crowd appear to outcompete the performance of the best doctor of the group in a diagnosis task in specific conditions [112,113]. Encouraging the request of peers' opinions while deciding could be another way of overcoming individual cognitive biases in clinical

medicine. However, to ensure its efficiency and avoid backfired effects, such solutions must be designed in a way that prevents social dynamics from negatively influencing individuals' own thoughts (authority bias, bystander effect...).

2.3.2. Adaptation of the environment to support decision-making.

In parallel to enhancing clinicians' sensitization and training, newly available evidence can help adapt the decision-making environment to promote the most optimal choices.

First, targeted debiasing could be mediated by cognitive aids, by adapting existing tools or conceiving new ones tailored for real-life needs and constraints, to minimize the number of errors caused by an inappropriate use of heuristics, for instance. Checklists can for example guide doctors and caregivers in carrying out medical procedures to avoid potential mistakes due to cognitive load, attentional limits or fatigue [114–117]. Moreover, frameworks have already offered to enhance and standardize handoffs in hospitals and their impact assessment resulted in a positive outcome [118,119]. Other tools such as fast-and-frugal decision-trees [120] can also facilitate optimal decision-making under uncertainty, whereas practical mnemonic aids can foster the recruitment of metacognitive thinking while facing complex clinical situations [121,122].

Beyond physical tools, new technologies bring many opportunities to produce and support medical decision-making. In recent years, the strength of machine-learning algorithms considerably increased, providing doctors with information based on extended datasets supporting diagnosis. As such, digital phenotype could for instance ease the diagnosis process in psychiatry by enabling to get an exhaustive picture of the patient's symptoms [8]. Even though these technologies sometimes outcompete experts' performance, professionals should exert caution when relying on digital insights: as such software is programmed and fed with data originating from "biased" humans, hence, they cannot be considered intrinsically objective [123]. Further research is needed to adapt machine-learning tools to doctors' cognitive mechanisms in order to improve their accuracy and reduce the risk of biases or misinterpretations [124].

Last but not least, in clinical medicine, a consequent portion of decisions is made by relying on complex information, and more specifically on statistical and numerical information. In order to carry out a diagnosis, prescribe a treatment or a medical

¹ <https://behaviouraleconomics.pmc.gov.au/projects/nudge-vs-superbugs-behavioural-economics-trial-reduce-overprescribing-antibiotics>

procedure, evaluate a prognosis, doctors reason and decide based on the diseases respective prevalence or the intrinsic cost/benefit ratio of each medication or operation. However, numerous studies suggest that humans are generally low-skilled at manipulating probabilities, as a significant part of identified cognitive biases interferes in this task. So-called statistical illiteracy was not only observed among lay people, but also among professionals having relevant expertise in their fields, including doctors [125,126]. The poor understanding of statistical information can lead to phenomena such as overdiagnosis and overtreatment tendencies, or to differential care choices based on irrelevant data. The solutions to overcome this problem can be of two types: teaching every professional how to better understand statistical information to improve statistical and numerical literacy, or adapting the communication to facilitate their processing [55]. Although both should be implemented, the second strategy will give quicker outcomes than the first. There are several insights to improve our communication of numbers to make the information more understandable. These strategies target the way statistical information should be framed: prioritize natural frequencies over probabilities, absolute over relative risks [127] and graphical representations over numerical information [128]. Making the information more digestible enables both caregivers and patients to make well-informed decisions, thus empowering the decision-makers [55].

In recent years, a growing number of research projects focused on developing promising, and often simple low-cost venues to mitigate the impact of cognitive biases in the medical context relying on different strategies and at various scales. Several units worldwide carried out multiple projects to implement behavioral science within health public policies and more specifically targeting practitioners (Commission Impact des Recommandations² from French National Health Authority). Going back to the example of scheme of decisions processes in neuroprognostication of consciousness disorders proposed above (*Figure 1*), the dissociation of the 2 processes, namely neuroprognosis and goal-of-care decisions, appears as a fundamental measure. This can implicate separate meetings, separate documents etc, that would mitigate the risk of wishful thinking. Group reasoning is also naturally used in these difficult processes.

However, such solutions cannot blindly be transferred from one context to another and call for a constant approach of impact

evaluation before implementation. Research about the impact of human factors in medicine should not overshadow structural detrimental conditions such as the lack of human resources or equipment. Recommendations based on individual improvements are only applicable and acceptable in a favorable and fair clinical environment where all necessary human and material prerequisites are met. Such behaviorally inspired practical interventions are not substitutes for minimal material required conditions for providing qualitative care to patients: they complement and support properly trained, rested and paid members of sufficiently staffed, fulfilled and equipped medical teams.

3. Call for further rigorous research

3.1. Available research: points of caution

3.1.1. Partial understanding or misuse of “cognitive bias”. The term “cognitive bias” appears self-explanatory and transparent: “distortions in the cognitive processing of information”, “a systematic deviation from logical and rational thinking” of which humans would be victims on a daily basis since they would lead to “errors of judgment or reasoning” (as definitions found in general dictionaries). If this widely used definition is not in itself incorrect, it does not completely cover the spectrum of what the notion of “cognitive bias” refers to in the scientific literature. Indeed, an essential aspect is lacking: generally speaking, cognitive biases constitute errors in a heuristics-based reasoning system that happens to be fully functional and efficient in many everyday situations. Here is an example: in the world we live in, observing a correlation between two events often leads people to infer a causal relationship between them. In some situations, this trait is likely beneficial, as it might enable individuals to better understand and interact with their environment (“If I go outside without my coat, I might get sick.”). However, combined with human’s tendency to seek, better memorize and give more credit to information confirming their initial idea (confirmation bias), it is not so surprising that we sometimes develop false beliefs by wrongly concluding that there is a causality (illusion of causality) between two elements that correlate but which in reality just share a common underlying factor. For example, people might believe in the efficiency of alternative medicine and pseudoscience because it made them feel better, despite the fact that time, immune response or placebo effect would have had the same effect [129–132]. The two elements perceived with a causality between them might even

² https://www.has-sante.fr/jcms/p_3085449/en/commission-impact-des-recommandations

have nothing to do with each other (as exposed in a recent paper highlighting the strong correlation between national football team FIFA ranking and total confirmed COVID-19 cases [133]). Despite the adaptiveness of heuristics, the common partial definition of “cognitive bias” only emphasizes on the fact that they occasionally lead to suboptimal outcomes or errors in some contexts, resulting in the view of a “biased”, “flawed” human brain, among both laypeople and specialists.

3.1.2. The bias bias. This prevalent focus on cognitive biases rather than heuristics as well as the dissemination of non-exhaustive nomenclature and lists of cognitive biases has developed a widespread tendency to explain complex behaviors by labeling them with one or more well-identified cognitive bias(s), leading to a simplification of reality. While the issue of human factors (and, among them, suboptimal cognitive mechanisms) in medicine is fundamental to explore for clinical practice improvement, it is also important to avoid falling into an over-interpretation tendency of the “bias bias” [36], and authors recently called for parsimony and normative principles in bias research [38,134]. During the COVID-19 pandemic, many articles have been published, both in the general press and in scientific literature, in order to decrypt humans’ “irrational” reactions and decisions towards the health crisis [135,136]. Citizens were for example described as being prone to optimistic bias, minimizing the rising risk at the beginning of the pandemic [137–139], whereas physicians were supposedly more likely to fall into cognitive biases pitfalls during diagnostic procedures due to COVID-19 disease prevalence [140]. Such global behavioral analysis might be influenced by the so-called hindsight bias: the human tendency to perceive past events as being more predictable than they actually were. Indeed, such a health crisis is characterized by a particularly high and long-lasting level of uncertainty that increases decision-making complexity. As uncertainty fades, looking back to find a posteriori explanations of the apparently “irrational” behavior citizens or professionals adopted through cognitive biases might lead to fallacious or potentially harmful conclusions if used to blame “biased” individuals or to make them endorse the full responsibility of adverse events.

In these perspectives, the study of individual cognitive biases and their impact in the medical context should not divert physicians’, researchers’ and decision-makers’ attention from monitoring and addressing other phenomena. As such, and as supported by Gigerenzer and colleagues, heuristics are valuable strategies to explore and refine to support reasoning and decision-making under uncertainty. Structural biases can also emerge from clinical environment practical settings and constraints while other social biases can arise from the asymmetric interactions between

individuals (health professionals and patients, for instance); these factors are also worth considering and investigating. Subsequent behaviorally inspired practical interventions are not substitutes for minimal material required conditions for providing qualitative care to patients: they should only complement and support trained and rested members of sufficiently staffed and equipped medical teams.

Despite these risks and pitfalls, this attractive concept of cognitive biases can shed light on the importance of evaluating human factors in many situations to mitigate their negative impact on clinical choices. These cognitive mechanisms should be explored in targeted real-life medical situations to better understand whether and how to act toward them.

3.1.3. Quality of current insights. Theoretical frameworks depicting cognitive mechanisms at stake in reasoning and decision-making under uncertainty point out the necessity to avoid several pitfalls when conducting experimental work “in the wild”. However, most of the available research on heuristics and cognitive biases and their impact in the medical context is conducted outside of this theoretical scope, often by clinicians themselves whose interest eventually got caught by the popular, attractive and (apparently) self-explanatory notion of cognitive biases. Research projects aiming at exploring these phenomena in practitioners’ own professional environment are often initiated without a proper dive into theoretical debates. Hence, exploratory studies frequently rely on paradigms that do not integrate important insights from the fundamental literature and reproduce critical pitfalls, resulting in evidence of poor robustness [35,141]. Among the identified pitfalls, protocols are often built within a perspective aiming at spotlighting precise cognitive biases, resulting in biased tasks and instructions for participants. Paradigms rely on a low-to-moderate number of trials, often based on short descriptions of situations rather than physical stimuli, and on stimuli or tasks with weak ecological validity and relevance towards real-life medical decisions. The experimental course of action usually excludes feedback and practice, preventing individuals to learn and improve. Finally, analysis performed on collected data can also be fallacious and lead to orientated conclusions and publication bias.

3.1.4. Guidelines for further research. In order to enhance the quality of evidence about the use of heuristics and the potential impact of cognitive biases in the clinical context, especially in neuroprognostication, improvements can be made at different scales. Aligned with the importance of a comprehensive exploration of the theoretical literature prior to any experimentation to integrate perspectives beyond the heuristics-and-bias approach, a particular attention should be devoted to the simple

heuristics research program. The associated publications indeed provide an enlightening framework to both understand and study reasoning and decision-making under uncertainty, through the prism of ecological rationality [35,142]. Among formulated recommendations, the authors developing these alternative approaches prescribe to increase as much as possible the adequation between chosen experimental tasks (including instructions, their framing and their difficulty) and the dilemma faced in the real-life environment, and between stimuli (both in nature and frequency), and available information “in the wild”. The experimental settings should be designed to ensure the reception of feedback by participants to foster learning, as it occurs in real-life. Overall, these recommendations invite to avoid off-ground, simplistic, biased or fallacious experimental designs, and to make experiments focusing on better depicting and understanding human reasoning and decision-making abilities under uncertainty more ecologically representative and relevant [35,80,141].

3.1.5. Clinicians’ metacognition, a promising avenue. The three most explored and identified cognitive biases in the medical context are the framing effect, biases linked to humans’ tolerance to risk/ambiguity, and overconfidence [80]. The study of this last phenomenon is particularly promising for several reasons. First, in a climate of uncertainty, decision-makers’ confidence in their own perception, knowledge, reasoning processes and ultimately, in their choices might be a key parameter to guide individuals’ behaviors through the decision-making journey. Hence, an appropriate perception of uncertainty and relevant associated confidence judgments could be a prerequisite to become conscious of the risk of error, promote the recruitment of the best-suited reasoning pathways and strategies, and foster the use of available decisional aids, leading to optimal outcomes. Second, among proposed solutions evoked to mitigate the extent to which cognitive biases affect medical decisions, and in order to minimize resulting errors, training clinicians’ metacognition has received a growing amount of attention [102,143]. This venue of action demonstrated real potential and received evidential support [68], albeit further research is still needed to refine recommendations to foster an appropriate use of this ability and to control for potential detrimental effects [73,108,109]. While being aware of the existence of an optical illusion often does not allow individuals to adjust their perception to the objective reality, knowing the diversity and prevalence of cognitive biases and their impacts on decisions might not allow to avoid these reasoning pitfalls. However, exerting metacognition in both situations by eliciting relevant confidence judgments could lead to the adoption of appropriate attitudes towards the situation, such as exercising caution, seeking additional information, double-checking, asking for help or being ready to consider alternative options before making the final call.

On the one hand, a substantial number of studies identified overconfidence at stake in the context of medical decision-making [73,80,81], but the results of these studies often suffer from critical pitfalls in their experimental design. On the other hand, sensitizing clinicians to the importance of training and using their metacognitive abilities offers encouraging evidence in mitigating the impact of human factors on medical decisions. Arising from these observations, a question remains: what is the current state and quality of knowledge about clinicians’ metacognition, and their confidence in medical knowledge and decision under uncertainty? How relevant are clinicians’ confidence judgments towards the actual accuracy of their decisions? From chasing overconfidence among caregivers, research should emphasize on studying clinicians’ confidence and, more broadly, metacognition, through robust experimental settings and methods. While providing care to patients presenting disorders of consciousness and as in many other medical situations, it is the healthcare providers’ and clinical system’s ethical imperative to exert professional conscientiousness and foster metacognition to minimize the risk of suboptimal choices by tailoring human factors to preserve patients’ safety from unfortunate consequences [144].

DECLARATIONS

Consent for publication. Not applicable.

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