

The challenge of mental simulation in preference-sensitive treatment decisions

Running title: Mental simulation in treatment decisions

Pighin Stefania*, PhD, & Tentori Katya, PhD

Center for Mind/Brain Sciences, University of Trento, Trento, Italy

* = Corresponding author

Stefania Pighin, CIMeC, University of Trento (Italy), Corso Bettini, 31, 38068 Rovereto (TN), Italy;
tel.: +39 0464 808622; email: stefania.pighin@unitn.it

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Imagine having just been diagnosed with cancer. While still feeling overwhelmed by negative emotions, such as sadness, fear, anxiety, etc., as well as by a massive amount of medical information about your condition, your doctor invites you to consider a number of therapeutic options. To compare them and to make an informed choice, you need not only to take into account your current clinical situation, but also to construct clear and accurate mental representations of the relevant future states associated with each of your possible courses of action. This means understanding, for example, the potential benefits and harms of the available treatments and determining, both in the short and long term, what side effects will most decrease your quality of life, what level of pain you will be able to accept, how your daily routine will be affected, and so on. The capacity to project the self forward in time and pre-experience what might occur in one's personal future is a specific form of reasoning known as *episodic future thinking* [1,2]. This prepares individuals for what is to come [3,4] and supports a range of cognitive processes, including emotion regulation, planning, and decision making [2].

Mental simulations of future personal events and related physical or psychological states are built by combining incoming information with stored knowledge [5-7]. They have been shown to be effective in prompting individuals' adaptive functioning in monetary choice tasks [8-10], inter-temporal choices in the domains of eating behaviors [11], alcohol and cigarette consumption [12,13], as well as prospective memory [14], which is the ability to remember to carry out a designated intention at some point in the future. (For extensive reviews on the frequency, content, and functioning of mental simulation obtained by behavioral and neuroimaging studies, see [5,6].)

Although mental simulations are generally considered deliberative, creative, and free of rules, they are actually subject to several constraints. Experimental findings indicate that inaccurate spontaneous prospective imagery may arise from four main sources [5]. First, since mental simulations are constructed from memories [15,16], and memories are biased toward the most salient (i.e. recent, unusual, or rare) elements of past experiences [17-19], it follows that mental simulations may be inaccurate as well [20]. Second, mental simulations tend to represent only a few moments of

the simulated events (such as the initial part), which are often strongly emotionally connotated. As a consequence, mental simulations are likely to overrepresent the moments of intense pleasure or pain, without taking into consideration emotional adaptation [21,22]. Third, mental simulations are typically too essentialized, in the sense that they include only a limited number of features of the simulated event, even though other factors can influence the hedonic value of future experiences [23]. Finally, mental simulations are often de- or mis-contextualized [24,25] as they overlook the impact of future physical and psychological conditions while, at the same time, overly accounting for current transient states, such as thirst, hunger, and fatigue.

The translational relevance of these studies to the medical practice has not yet been fully explored. Sparse empirical findings suggest that patients' preference-sensitive treatment decisions may suffer due to the pitfalls of spontaneous mental simulation.

For example, with regard to the first source of error in mental simulation; previously described, the effect of unrepresentative memories on patients' willingness to undergo invasive medical examinations again [26] has been attributed to biased mental simulations of the associated discomfort [5]. However, it is unclear to what extent these findings can be generalized to other invasive medical procedures (such as a bone marrow aspiration or a cervical biopsy) and how these results can be used to improve patients' adherence to follow-up. The picture is further complicated by the fact that patients are often required to envision themselves in future scenarios that they have never experienced before. In the absence of first-hand knowledge, they cannot rely on their episodic memory in order to imagine what might plausibly occur but rather must create a representation by integrating incoming information (e.g., the details of therapy, the magnitude of possible side effects) with their semantic knowledge. On the one hand, this is likely to make a realistic and detailed picture more difficult to achieve and might increase patients' susceptibility to being overwhelmed by technical details; on the other hand, it may prevent them from being too anchored to past experiences that won't necessarily recur in the future.

Healthy people's incorrect appraisal of disabled or chronically ill individuals' well-being is evidence of the second source of error in mental simulation. This has been ascribed to a general overestimation of the immediate impact of potential declines in health, an overestimation that ignores the tendency of various emotional reactions to dissipate over time and/or to be replaced with others [5,27]. Unfortunately, to date, empirical attempts to defocus people's mental simulations from the immediate impact of health changes, by means of exercises that induce reflection on domains that may not be affected by the health change itself, have proven unsuccessful [28,29]. Accordingly, the understanding of the factors that contribute to discrepancies in ratings of health states between healthy people and patients is far from complete.

Possible implications of the last two causes of biases for episodic future thinking in the clinical domain are still being fully explored. Indirect evidence seems to suggest that essentialized and de- or mis-contextualized mental simulations may affect treatment decisions. For example, it has been reported that a major source of patients' long-term regret is their underestimation of possible side effects at the time of the treatment decision [30-31]. One explanation for this could be a general tendency, when selecting the treatment for a serious illness, to focus almost exclusively on the effectiveness of the treatment in curing the disease, without taking into sufficient consideration other aspects (e.g., adverse effects, treatment cost or duration.) [32].

Finally, the effects of patients' emotions under distress (such as fear and feelings of uncertainty) on treatment preference decisions [33] suggest that the prediction of future hedonic conditions is based almost exclusively on current states, while ignoring the transience of most emotional reactions [34-35]. However, yet again, the hypothesis that relevant aspects of the treatment decision are missing from patients' mental simulations because they are considered nonessential or vitiated by temporary contextual factors is, at the moment, mainly speculative and well worth exploring in the future.

Cognitive research has sought to identify how mental simulations impact expectations (e.g., on the perceived valence or plausibility of future events) and what factors can improve prediction

accuracy. The results suggest that prospective judgments benefit from prompting individuals to broaden the number and type of alternative scenarios generated so that they can access additional information about ways in which future events may unfold. In this regard, two debiasing techniques that have been proved effective in laboratory settings consist of encouraging individuals to construct representations of the best- and the worst-case scenarios for each available course of action and/or to envisage themselves acting within each detailed, generated scenario (e.g., to specify what actions will be performed, when and where) [see 1,36-38].

To conclude, although we all commonly engage in mental simulation [39], our spontaneous episodic future thinking is generally limited by various cognitive constraints [5]. Patients are no exception and are likely to incur all the problems outlined above when facing treatment decisions. A more accurate exploration of patients' spontaneous imaginative thoughts, together with the development of procedures to overcome, or at least limit, their most common errors would then constitute, in our opinion, an important step towards the goal of optimal treatment. In particular, patients' deliberative processes could benefit from health professional support aimed at promoting and guiding their construction of comprehensive and detailed representations of what might affect their well-being and satisfaction during the various phases of alternative courses of action. This would require not only defocusing patients' attention from their current negative emotional states and explaining to them all implications of their conditions and treatment options, but also nudging patients to actively engage in a detailed simulation of relevant possible future events that also includes those aspects typically neglected by non-experts. Such support would ideally be provided as routine practice in physician-patient interaction between diagnosis and treatment choice. Hopefully, in the long run, a greater understanding of how to make use of appropriate mental simulations in the clinical domain together with the development of targeted debiasing techniques as those abovementioned could not only allow for a more thorough consideration of patients' preferences but also foster their decision-making autonomy.

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