A psychophysical account of patient non-adherence to medical prescriptions.
The case of insulin dose adjustment

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Abstract

\textbf{Aim.} – Diabetic patients often do not adjust their insulin doses using the algorithms that they have been taught. While this behavior may intuitively have a number of causes, such as the complexity of the decision or the fear of hypoglycaemia, we propose in this article a more general, “psychophysical”, explanation based on behavioral economics concepts used to describe decisions made under uncertainty and risk. The concepts discussed herein may not be familiar to clinicians, who will find here an introduction to theories that may be helpful in understanding some aspects of non-adherence to medical prescriptions.

\textbf{Results.} – 1) The Prospect Theory of Kahneman and Tversky proposes that choices made in the context of risk are subject to loss aversion. 2) Decisions under uncertainty use mental short cuts called “heuristics”, which can lead to biases; for instance, overestimating the probability of the risk. 3) To understand the very concept of risk, emotions must be considered with a special focus on anticipated regret. 4) Finally, selection difficulty is an important determinant of the preference for the status quo.

\textbf{Conclusion.} – These concepts may be relevant for understanding a preference for the status quo in decisions made in a context of uncertainty and risk, such as insulin dose adjustment. We suggest that these mental mechanisms may also be involved in other aspects of patients’ non-adherence. As other common human behaviors, non-adherence may actually often be a consequence of biases resulting from our ways of thinking, being both cognitive and emotional, and, according to Kahneman, more often “fast” than “slow”. Empirical studies are needed to support this hypothesis.

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Keywords: Diabetes; Insulin therapy; Treatment; Loss aversion; Heuristics; Prospect Theory; Non-adherence; Psychophysics

Résumé

Une interprétation psychophysique de la non-observance thérapeutique. Le cas de l’adaptation des doses d’insuline.

\textbf{But.} – Il arrive souvent que les patients diabétiques n’adaptent pas leurs doses d’insuline selon des algorithmes qui leur ont été enseignés. Bien qu’on puise comprendre intuitivement que ce comportement puisse avoir de nombreuses causes telles que la complexité de la décision ou la peur de l’hypoglycémie, nous proposons dans cet article de considérer une explication plus générale, « psychophysique », relevante de l’économie comportementale qui décrit les décisions prises dans un contexte d’incertitude et de risque. Les concepts discutés ici peuvent ne pas être familiers pour les cliniciens qui pourront y trouver une introduction à des théories pouvant être utiles pour comprendre certains aspects de la non-observance.

\textbf{Résultats.} – 1) La Théorie des Perspectives de Kahneman et Tversky propose que les décisions prises dans un contexte d’incertitude et de risque sont sujettes à une aversion pour les pertes. 2) Elles utilisent des raccourcis mentaux, appelés « heuristiques » qui peuvent conduire à des biais, par exemple en surestimant la probabilité des pertes. 3) Pour comprendre le concept même de risque, il faut prendre en compte les émotions, avec une attention spéciale pour le regret anticipé. 4) Enfin, la difficulté du choix est un déterminant important de la préférence pour le statu quo.

\textbf{Conclusion.} – Ces concepts peuvent aider à comprendre la préférence pour le statu quo dans les décisions prises dans un contexte d’incertitude et de risque, dont l’adaptation des doses d’insuline représente un exemple. Par conséquent, ces mécanismes mentaux peuvent être également impliqués dans d’autres aspects de la non-observance : comme d’autres comportements humains, celle-ci peut en fait être souvent la conséquence de biais résultant de notre manière de penser, à la fois cognitive et émotionnelle, et, d’après Kahneman, plus souvent rapide que lente. Des études empiriques sont nécessaires pour tester cette hypothèse.

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\textbf{Mots clés} : Diabète ; Insulinothérapie ; Traitement ; Aversion pour les pertes ; Heuristiques ; Théorie des Perspectives ; Non-observance ; Psychophysique

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Any diabetes education program teaches patients algorithms to adjust insulin doses based on the results of the Self-Monitoring of Blood Glucose (BG) [1]. These are typically “if-then rules”, such as: “If on three consecutive days you observed that your post-meal blood glucose is high, then you should increase the corresponding insulin dose”. It is a common observation that, despite knowing these rules, patients often do not use them under real life conditions [2] and instead maintain the same insulin dose while their blood glucose level is high [3]. There are other situations leading to decision avoidance:

- the “faked” diary, in which the BG written is lower than the reality [4]: because the BG is “normal”, there is no reason to make the decision of increasing the insulin dose;
- decision avoidance can also result from the absence of BG testing: one may wonder whether this behavior is not actually aimed at avoiding what would be a difficult decision [5].

The preference for the status quo is often observed for any decision made by human beings under circumstances of uncertainty and risk. According to Kahneman and Tversky, “a typical riskless decision concerns the acceptability of a transaction in which a good is exchanged for money, while the paradigmatic example of a decision under risk is the acceptability of a gamble that yields monetary outcomes with specified probabilities”[6]. Because insulin dose adjustment belongs to the second category, the aim of this article is therefore to draw from the psychological literature some explanations of decision avoidance and to propose that these explanations may be relevant for understanding the specific case of insulin dose self-management by diabetic patients and, more generally, some aspects of patient non-adherence to medical prescriptions.

More precisely, we will attempt to apply to these issues the “psychophysical” conceptual framework largely developed by Kahneman and Tversky, making a distinction between the normative solution to a problem and the subjective answer given by real-world individuals. Some of the examples used to illustrate the theories described in this paper have been taken from the behavioral economics literature, which may seem far from the diabetes field. However, these examples are taken from everyday life: we suggest that they have their counterpart in insulin dose adjustment, or, more generally, in adherence to therapies, which are also part of the patients’ everyday life.

1. The normative solution: The calculus of the Expected Utility Theory, applied to insulin dose adjustment

Suppose a patient with a BG that is not in target and to which she attributes a value (a “utility”) of 0.4 (let us suppose that 1 would represent a perfect BG level and 0 that of an extreme BG level). If she decides to do nothing, she can expect that the utility will remain the same: 0.4. If she decides to modify the insulin dose, there are three possibilities: no change (the utility remains 0.4), a good outcome, or a bad outcome, with respective utilities of, says, 0.8 and 0.1. If she estimates that the probabilities of getting the good, no change, or bad outcomes are 0.6, 0.1 and 0.3, respectively, she can calculate an expected utility of changing the dose, which will be the sum of the expected utilities of the three possible outcomes, calculated as the product of their utility by the respective probability. In this example, the expected utility of changing the dose would be \(0.6 \times 0.8 + 0.1 \times 0.4 + 0.3 \times 0.1\), i.e. 0.55. Because this value is higher than that expected from the status quo (0.4), she should decide to change the insulin dose.

2. Psychophysics of decision: The Prospect Theory and loss aversion

Prospect Theory [7] was developed at the end of the 1970s by Daniel Kahneman and Amos Tversky. Their “psychophysical” analysis of outcomes was based on the observation that people usually do not behave according to the predictions of the calculus described above. For instance, when individuals are offered a choice between A: a sure chance of 500 € and B: a 50% chance of getting 1000 € and a 50% chance of getting nothing, most people prefer the certain gain, although the expected utility is the same. The observed behaviors are actually subtler. People were asked to choose between Gamble A: a 100% chance of losing $3000, and Gamble B: an 80% chance of losing $4000 and a 20% chance of losing nothing. Ninety-two percent of the participants chose B. Next, the participants had to choose between Gamble C: a 100% chance of receiving $3000, and Gamble D: an 80% chance of receiving $4000 and a 20% chance of receiving nothing. Only 20% of the participants chose D. Thus, people seem to seek risks in prospects involving losses, while they are risk averse to prospects involving gains.

Fig. 1 represents a summary of this theory. According to Kahneman and Tversky [6], “the key assumption is that the psychophysical analysis of outcomes should be applied to gains and losses from a reference point rather than total assets. Subjective value is a concave function of the size of a gain: the difference between the utilities of 200 and 100 € is greater than the utility difference between 1100 and 1200 €. The same generalization
applies to losses as well; the difference in subjective value between a loss of 100 and 200 € is greater than the utility difference between a loss of 1200 and 1100 €: the value function is convex in the domain of losses. The function is considerably steeper for losses than for gains. This loss aversion expresses the intuition that a loss of X € is more averse than a gain of X € is attractive”.

This theory may be relevant for the issue of insulin dose adjustment: just consider the loss aversion effect on weighing the risk of hypoglycaemia (loss) vs. the gain linked to achieving a better BG.

3. Decision under uncertainty: the concept of heuristics

Heuristics are simple, efficient procedures that help find adequate, though often imperfect, answers to difficult questions. Heuristics explain how people can make decisions in a context of uncertainty. Heuristics work well under most circumstances, and this may explain their evolutionary development, but in certain cases they lead to systematic errors or cognitive biases [8]. Gilovich and Griffin [9] illustrate one of these heuristics described by Kahneman and Tversky [10], known as the availability heuristic, with the following example: if you are asked to evaluate the relative frequency of cocaine use in Hollywood actors, you may instead assess how easy it is to identify examples of celebrity drug-users. Heuristics actually consist of substituting one question for another, which can be a good strategy for solving a difficult problem [8].

We saw above that the loss aversion predicted by the Prospect Theory may lead to a bias in estimating the respective utilities of the outcomes, which may result from the patient’s decision of changing or not changing her insulin dose. Here, using the availability heuristic may introduce a bias in estimating the respective probabilities of occurrence. For instance, if you try to evaluate the relative risk of hypoglycaemia after increasing the insulin dose, you may assess how easy it is to identify examples of hypoglycaemia in your past experience. It may be easier to retrieve examples of hypoglycaemia than normo- or hyperglycaemia (which is usually asymptomatic) due to the greater power of bad events over good ones on learning processes [11].

This effect leads us to consider the effect of emotions (i.e., fear), as it is well known that emotions are involved in the memory process [12].

4. Emotions and decisions under risk

4.1. Emotions are encompassed in the very concept of risk

Loewenstein et al. noticed that in a traditional model of decisions made under conditions of risk, primarily “consequentialist” (individuals make up their mind by appreciating the consequences of their choice), emotions would be essentially regarded as epiphenomena [13]. These authors proposed a “risk-as-feelings hypothesis” where feelings play a causal role in behavior under risk conditions. They introduced a distinction between anticipatory and anticipated emotions. The former are immediate, visceral, effects; for example, the fear, anxiety or dread that one feels when one has to complete an action that presents a risk.

The anticipated emotions are not felt immediately, but are those that one imagines one is likely to feel as a consequence of the decision. For instance, the importance of anticipated regret in decision-making can be demonstrated by the following empirical study: Imagine a $100 sky pass and three groups of participants. The participants in Group 1 missed a hypothetical opportunity to buy the sky pass for $40. Those in Group 2 missed an $80 price. Group 3 had no initial opportunity. All of the participants then had the opportunity to buy a pass for $90. The participants in Group 1 rated themselves as least likely to purchase the ticket. These results can be explained by regret avoidance (regret would be more important in Group 1) [14].

Loewenstein et al. proposed a model in which individuals evaluate the possible outcomes of a choice at risk in a cognitive way, as in the traditional model, by taking into account the desirability and the probability of the outcome (typically the “expected utility” discussed above); anticipated emotions are part of the outcome. This cognitive evaluation has consequences, including emotions that interact with the results of the cognitive evaluation. Moreover, there are anticipatory “feelings” that can also be triggered in a fast, non-cognitive, way depending on the context. This “risk-as-feelings hypothesis” proposed by Loewenstein et al. therefore represents a description of rationality with two distinct pathways that can possibly be contradictory.

It is easy to adapt this description of the decision-making process to what is at stake in insulin dose adjustment: first, as discussed above, the cognitive evaluation of the outcome can be biased by the availability heuristic, increasing in the mind of the patient the perception of the risk for hypoglycaemia, the “most feared complication of insulin therapy” [15]; second, the fear of hypoglycaemia can be involved both in the anticipated and the immediate, anticipatory, modes of emotions.

4.2. Emotions and behavior: rather than causation, a feedback dynamics

The preceding model seems to give emotions a causal power on behavior. Baumeister et al. [16] proposed another model, in which emotions influence behavior as feedback: suppose that a given behavior, following the application of an “if-then rule”, leads to an unpleasant outcome, inducing the occurrence of a strong negative emotion. The next time this rule will have to be applied, a short recollection of this feeling will occur like a flash, helping the individual avoid the same mistake. It thus appears in this model that the role of the emotions, as opposed to what one intuitively believes, is not to cause the behavior, but to shape the cognitive process. Baumeister et al. noticed in an elegant way that one can understand, within the framework of this model, why one cannot control emotions: you cannot control emotions because the role of emotions is precisely to control you. This explains the “near-miss effect”: there is more emotion after just missing your train by a few minutes than after missing it by half an hour. It is important that you remember this story vividly: if you miss your train by 3 minutes, then you may profitably regret
dawdling over your second cup of coffee; next time, you will skip this second cup and make the train. The emotions represent therefore a system of feedback, the goal of which is to provide training and control behavior.

Again, this model may also be useful in describing the emotional process at stake in the avoidance of insulin adjustment linked to the fear of hypoglycaemia. Having to increase insulin in the face of a high BG value, the recollection of a previous hypo leads the patient to reconsider the use of the “if-then” rule. We can therefore understand how a past history of severe hypoglycaemia can have a major effect on patient use of “if-then” insulin adjustment rules and, more generally, patients’ attitudes concerning diabetes management. For instance, shortly after the publication of the DCC Trial, 330 of the 550 patients interviewed declared that they felt encouraged to improve glycaemic control. The factors associated with a low desire to improve blood glucose levels included a history of severe hypoglycaemia [17].

On the other hand, emotions may be instrumental in enabling people to learn [18,19], as shown by the near-miss effect mentioned above. In our context, the fear experienced after a severe hypoglycaemic episode may be a part of the learning process leading the patient, by counterfactual thinking (counterfactuals are thoughts about alternatives to past events, that is, thoughts of what might have been) [20], to avoid the circumstances causing hypoglycaemia in the future.

5. The concept of selection difficulty

In a review entitled “The Psychology of Doing Nothing” [21], Anderson proposed a “rational-emotional” type model very close to those previously described, implying the role of loss aversion (cf. the Prospect Theory) and regret as anticipated emotions and finally a concept obviously interesting for our subject: selection difficulty.

For Anderson, the fact that one finds decisions difficult is not equivalent to the feeling of uncertainty: he gives as an example the student who forgot his pencil the day of the examination and must choose between the two types of pen proposed to him; he does not know which is the best but will not find it difficult to make a decision. The difficult decision is not one which evokes intense emotions: the virologist who is facing an extremely serious epidemic and must decide between two treatments with the same cost, but one will save 1.5 and the other 4% of the population, is placed in a strongly emotional situation but will not find it difficult to make a decision. On the other hand, a difficult decision can be seen even in the absence of uncertainty or emotion, although uncertainty and emotions are associated with the difficulty of the decision.

Among the many factors discussed by Anderson in his review as making a decision difficult and leading to inaction in general, one can retain the following: the difficulty in adopting a clear strategy due to a lack of time, the multiplicity of options, the uncertainty of preferences, the fact that the choice is badly defined, perhaps the personality of the agent, or even her culture.

Again, it is easy to apply these concepts to the specific case of insulin dose adjustment, leading to a preference for the status quo. An algorithm cannot be perfect and applicable to any situation, and patients often may not follow an algorithm because there are too many variables that are not employed in the algorithm, e.g., the combined effects of stress, exercise, certain foods, illness, etc., on blood glucose: patients appropriately take the decision to override the algorithm based on previous experience. This “intuitive” explanation is consistent with the concept of selection difficulty described above [21]. Incidentally, one may see functional insulin therapy, which provides patients with simple algorithms based on insulin-glucose and insulin-carb coefficients, as a tentative to provide a simple answer to a complex question.

6. The role of “if-then” rules in the patients’ progression towards expertise

It may be relevant to evoke the five-stage novice-expert pathway model proposed by Dreyfus and Dreyfus [22]: in the “novice” stage, there is rigid adherence to the taught rules or plans with little situational perception and no reference to context. Next, the “advanced beginner” uses guidelines for action based on “aspects” (global characteristics of situations recognizable after some prior experience). Becoming “competent”, he now sees actions at least partially in terms of long-term goals. The next stage is that of “proficiency”, where he sees situations holistically rather than in terms of “aspects”. Finally, the true “expert” no longer relies on rules or guidelines, but on an intuitive grasp of situations based on deep, tacit understanding. At that stage, analytical approaches are used only in novel situations or when problems occur.

We would like to suggest that “if-then” insulin dose adjustment rules are therefore mostly helpful at the beginning, during the first step of the pathway moving from novice to expertise. However, we noted that patients often do not use these rules. This behavior may therefore represent an obstacle to their progression towards real expertise in diabetes management, pointing out the importance of elucidating the mechanisms of the preference for the status quo, which was the aim of this article.

Incidentally, these considerations may be useful in understanding how patients may benefit from modern glucometers, which can become real “decision tools”, although their value deserves thorough evaluation: glucometers should:

- save time because a lack of time leads to inappropriate risk evaluation;
- fight against uncertainty by providing blood glucose trends, thus making decisions easier, or;
- even make decisions for the patient [23], if possible explaining the rationale of the decision and participating in patient education.

However, it is important that providing patients with information does not exaggerate the degree of negative emotions, especially fear.

7. Discussion

These concepts may shed new light on intuitive explanations for a preference for the status quo, which is often observed in
insulin dose adjustment: first, we have to admit that, as shown above, insulin dose adjustment typically represents a “difficult decision”. In addition, it is important to note the fact that glucose regulation is a non-steady state model; for instance, it is well known that intestinal carbohydrate absorption, the resorption of insulin depots after an injection in the subcutaneous tissue and, more generally, the glucose distribution in the body and metabolic rates of glucose inputs, outputs and exchanges from one compartment to another are subject to day-to-day fluctuations. Moreover, even the most physiological insulin regimens are poor imitators of the pancreas: indeed, insulin dose adjustment cannot be as successful as a minute-by-minute regulation of blood glucose. Thus, all of the phenomena that normally participate in glycaemic control are depending on stochastic processes governed by probabilities, and one should not wonder that patients have difficulty in making a decision and prefer the status quo. Again, these remarks represent a major argument to examine how people make decisions in a context of uncertainty and risk. As proposed by Kahneman and Tversky, in general, “people are not good intuitive statisticians”: confronted with a difficult decision, people will not make calculations but use heuristics.

Second, a fear of hypoglycaemia is usually the first explanation given to explain why patients do not adjust their insulin doses [3]. In a previous study, we collected 86 pages of diabetes diaries representing 1690 decisions from type 1 diabetic patients. We returned the pages to the patients after having deleted the insulin doses and asked them what their decisions would be. We observed that patients in real life conditions changed their insulin doses less frequently than they would in the framework of a theoretical exercise. The fact that the main change occurred for the decisions involving an increase in the insulin dose was consistent with a role for the fear of hypoglycaemia [24]. These empirical data are at least consistent with the involvement of the mental mechanisms described in this paper, and we suggest that this framework should pave the way for additional studies aimed at more specifically supporting the roles of loss aversion and anticipated emotions in patient non-adherence to insulin dose adjustment recommendations.

Finally, the emphasis given in this article to the role of emotions, and specifically the role of fear, is also consistent with the different steps of a “fear cycle”: the fear of hypoglycaemia leads to poor glycaemic control, which in turn is a causative factor for guilt and fear of diabetic complications. The latter results in the patient’s distress, which in turn aggravates the fear of hypo-glycaemic episodes, thus closing the loop. We suggest that this vicious cycle may be amplified by the loss aversion effect.

8. Conclusion

This theoretical analysis is largely based on the psychophysical concepts summarized by Daniel Kahneman in his recent Thinking, Fast and Slow [8], which suggests that our thinking process is made up of two systems. System 1 (Thinking Fast) is unconscious, intuitive and effort-free. System 2 (Thinking Slow) is conscious and requires effort. Theoretically, these concepts should be relevant in helping us understand some patients’ health behaviors.

In this article, we specifically considered insulin dose adjustment because it represents the paradigmatic example of risky decisions that empowered patients are supposed to make within the framework of their treatment. However, we suggest that the hypothesis described herein may have implications for patient adherence mechanisms in general. We previously proposed that patient non-adherence to medical prescriptions in chronic diseases may result from a “myopic” preference for a small but immediate and concrete reward, rather than large but abstract and long-term benefits [25]. We also recently suggested that some patients may be non-adherent as a sign of disobedience [26], with non-adherence being a manifestation of reactance [27] (based on this psychological concept [28], an individual who feels that her freedom is threatened can refuse to be adherent simply because what one proposes was prescribed).

In addition to these mechanisms, we propose herein that the psychophysics of loss aversion and the involvement of emotions applied in this paper to the specific issue of insulin dose adjustment may also be involved in other aspects of non-adherence to medical prescriptions when they are perceived by patients as having a potential immediate risk. This leads us to propose a “psychophysical account” of patient non-adherence to prescribed therapies (Fig. 2): first, according to the Prospect Theory, aversion for immediate losses is greater than attraction for immediate gains; second, using the availability heuristic may lead to an overestimation of therapy-linked risks. Finally, these mechanisms may explain in part the paramount importance of anticipatory (immediately felt) and anticipated emotions in patient behavior regarding decisions concerning their health.

In a recent paper, Umar et al. published evidence that when patients evaluate their preferences concerning the
different attributes of a psoriasis therapy, the magnitude of their preference scores for the least preferred attribute was consistently higher than the magnitude of the mean scores for the most preferred one, suggesting that patients are not only concerned about receiving the preferred treatments, but perhaps are more concerned that the treatments with strong disutility not be recommended [29]. For the authors, who refer to a paper by Schwartz et al. [30], these data are consistent with the predictions of the Prospect Theory.

We suggest that loss aversion may not only be involved in patient preference for different therapies but also in their subsequent adherence. A 2008 review noted the fact that the Prospect Theory had not been empirically applied to the specific issue of medication adherence [31]. There is therefore a need for empirical studies aimed at testing the general hypothesis that patient non-adherence, like other common human behaviors, is actually often the consequence of biases resulting from our way of thinking, which is both cognitive and emotional and more often “fast” than “slow” [8].

Disclosure of interest

Professor Gérard Reach has received honoraria for giving lectures in symposia organized by Lifescan, Abbott, Roche Diagnostics, Bayer Diagnostics, and Menarini, all manufacturers of glucometers. He has served on the advisory boards of Lifescan, Abbott, Roche Diagnostics, and Bayer Diagnostics. He also received a grant from Lifescan for evaluating an educational tool used in functional insulin therapy.

References