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Applying principles from Game theory to Stroke Care

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Applying principles from the game theory to acute stroke care: Learning from the prisoner's dilemma, stag-hunt, and other strategies

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Abstract

Background: Acute stroke care represents a challenge for decision makers. Decisions based on erroneous assessments may generate false expectations of patients and their family members, and potentially inappropriate medical advice. Game theory is the analysis of interactions between individuals to study how conflict and cooperation affect our decisions.

Aims: We reviewed principles of game theory that could be applied to medical decisions under uncertainty.

Summary: Medical decisions in acute stroke care are usually made under constrains: short period of time, with imperfect clinical information, limit understanding about patients and families' values and beliefs. Game theory brings some strategies to help us manage complex medical situations under uncertainty. For example, it offers a different perspective by encouraging the consideration of different alternatives through the understanding of patients' preferences and the careful evaluation of cognitive distortions when applying 'real-world' data. The stag-hunt game teaches us the importance of trust to strength cooperation for a successful patient–physician interaction that is beyond a good or poor clinical outcome.

Conclusions: The application of game theory to stroke care may improve our understanding of complex medical situations and help clinicians make practical decisions under uncertainty.

Keywords

Acute stroke therapy, decision making, decision neuroscience, endovascular, game theory, neuroeconomics, outcomes, prevention, prisoners' dilemma

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> "If people do not believe that mathematics is simple, it is only because they do not realize how complicated life is".
> John von Neumann (mathematician considered the pioneer of game theory, 1903–1957)

Background

Many aspects of our everyday life require the ability to make decisions effectively. Typical decisions are characterized by multiple options, each carrying potential risks, rewards, and associated outcomes.[1,2] In economics, *uncertainty* is a term that comprises risk and ambiguity. *Risk* is used to describe situations of known probability.[3] For example, the risk of stroke among patients with atrial fibrillation and a CHADS2 score of 5 ranges from 8 to 17%.[4] In contrast, *ambiguity* is a term reserved for situations when probabilities are unknown.[3]

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Most difficult medical decisions require an estimation of the expected outcome under (sometimes inevitable) uncertainty. Decisions are commonly approached in two ways, intuitively (fast) or deliberately (slow).[5] Decisions based on erroneous assessments may generate false expectations of patients and their family members, and potentially inappropriate medical advice.[6] Stroke care is no exception in that respect.[7]

Game theory is the study of interactions between individuals (and even Nations) applying mathematical models of conflict and cooperation.[8,9] Game theory has been successfully applied to solve social situations under uncertainty. Some examples include conflicts in business negotiations, actions, salary negotiations, poker playing, and more intuitively in routine daily social interactions.[10,11] Limited information is available on the application of game theory to medical decisions.

The goal of this article is to introduce basic concepts of game theory to general physicians who had no prior exposure to this topic. We first summarize relevant principles in neoclassical economics, then concepts of the game theory and cognitive distortions, and finally introduce a practical case to illustrate its potential applications to acute stroke care. Using acute stroke care as an example, our aim is to introduce the game theory framework as a tool for allowing clinicians to make better decisions.[1,9]

A common case scenario

Part I: A 79-year-old retired banker developed right sided weakness and aphasia while at home. He arrived at the emergency department 125 min after symptom onset. On examination, he was arousable, had a left MCA syndrome consisting of a severe right hemiparesis, hemisensory loss, hemianopia, and global aphasia (NIHSS = 22). He was afebrile with a blood pressure of 178/92 mmHg and heart rate 102 beats/min.

A CT scan of the head revealed an ASPECTS (Alberta stroke program early CT score) of 6. There was a 10 mm hyperdense sign in the left middle cerebral artery on the plain CT. Past medical history includes hypertension, diabetes, cardiac failure, and a recent diagnosis of atrial fibrillation. There were no contraindications for intravenous thrombolysis (tPA). The treating physician initiated discussion with the family for starting intravenous tPA and consideration for endovascular treatment.

The evolution of classic economy theory

Blaise Pascal (1623–1662)—mathematician and scientist—introduced the concept of "expected value." He claimed that each decision maker compares simple numbers.[1] For example, in a lottery game that yields a 50% chance of winning US$ 100 or a certain US$ 30, participants should chose the option with the highest expected value. This could be estimated by multiplying the value (e.g. 100) by the probability (50%). However, Pascal's approach did not take into account the context or wealth function. For example, let us consider a poor man with a 50% probability of winning a lottery ticket of US$ 20,000. A wealthy man offers to buy that lottery ticket for US$ 7000. Based on Pascals' theory, the poor man should not accept the offer as the expected value of his ticket is higher ($20{,}000 \times 0.5 =$ US$ 10,000) than the expected value of the offer (US$ 7000). However, US$ 7000 may have higher utility function for him than the probability of winning a higher amount (or the expected value of US$ 10,000). In 1738, Daniel Bernoulli (Swiss mathematician and physicist) introduced the concept of "expected utility" using a mathematical transformation by correcting the expected value to account for differences in the current status (e.g. wealth). Bernoulli proposed a fixed logarithmic utility function and asserted that reasonable choosers should maximize that function. Thus, the satisfaction of decision makers declines by an additional dollar as a logarithmic function of total wealth. In addition, this function allows the differentiation between risk-averse and risk-seeking individuals.[12]

In 1928, John von Neumann (mathematician, physicist) published a simple mathematical theorem to demonstrate that two perfectly logical adversaries can arrive at a mutual choice of game strategies. His subsequent collaboration with the economist Oskar Morgenstern in the early 1940s resulted in the groundbreaking book *Theory of Games and Economic Behavior* developing the concept of individual choice in situations of risk that set up the foundations of game theory.[13] Perhaps, Von Neumann's major contribution was his vision on the integration of his mathematical work to physical and social sciences. The story gets more interesting when the concept of *revealed preference* was introduced in 1938 by the American economist and Nobel prize winner Dr Paul Samuelson.[1,14] Individuals may not know what would be the best choice. However, by observing people's choices we can learn about the given utility (assigned value to that choice). This approach provides an opportunity to better understand people preferences and risk aversion for events with low and high probability of occurrence.[1]

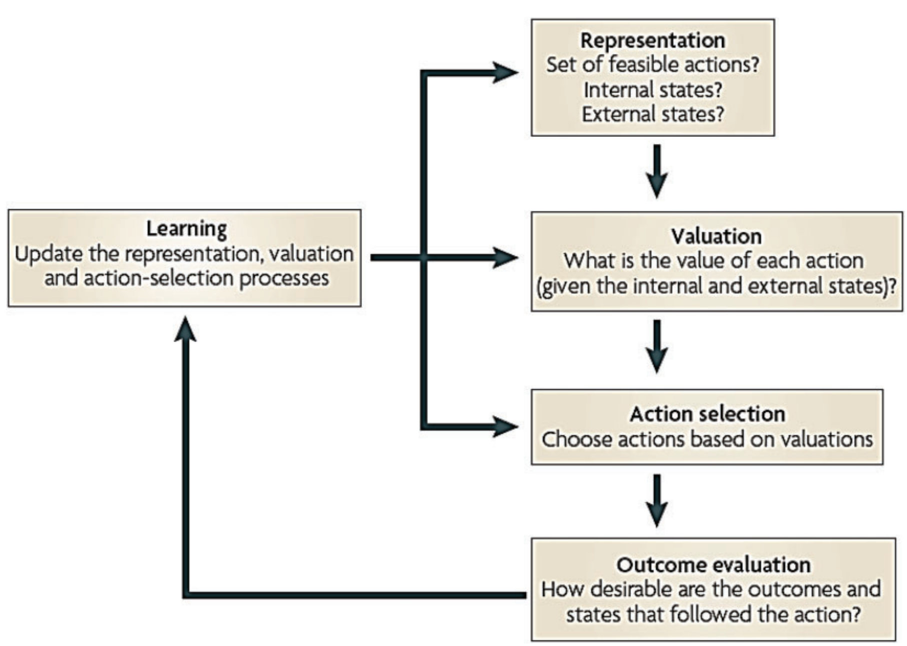
Decision neuroscience—also known as *Neuroeconomics*—is the field that studies how we make decisions.[1] We choose among alternatives based on our preferences to reach the best possible outcome. This is a hard-wired process that began as a way to satisfy basic instincts. Examples range from animals foraging and reproduction to more complicated human decisions, such as stock market trading or choosing the best clinical treatment option.

Brain steps in decision making

In the last decade, several advances were made in decision neuroscience that provided key advances in understanding how we make decisions. A framework illustrating different factors influencing our decisions is represented in Figure 1. In brief, value-based decision making can be summarized in five basic processes: first, the construction of a representation of the decision problem, which depends on our internal (e.g. satiety, thirsty) and external (e.g. environment) states; second, the valuation of the different actions under consideration; third, the selection of one of the actions on the basis of their valuations; fourth, after implementing the decision we need to measure the desirability of the outcomes that follow; and finally, the outcome evaluation is used to update the other processes to improve the quality of future decisions (called "prediction error").[15] As mentioned, we make choices to maximize the probability of achieving a good outcome based on the value we assign to different alternatives. A simplified approach in the understanding of the intrinsic steps is the consideration of a brain circuit with connected "stations," each encoding specific information about action value, expected reward, prediction errors, and expected utility.[15] A detailed explanation of the brain representation of the anticipated and experienced value, as well as expected reward, is beyond the scope of this article and has been described extensively elsewhere.[1,3,16] These stations can be cut short leading to heuristic errors—also called *cognitive distortions or bias*. The origin of most of our biases arises from shortcuts that can be allocated to one of these steps.

In the clinical domain, this system allows us to process and apply the available medical information from observational studies, randomized trials, and meta-analysis to be able to ameliorate the uncertainty and be able to estimate the risk in a particular scenario. Simple decisions are usually intuitive, repetitive, automatic, routine and hard-wired "programmed," and encoded in our brains based on our knowledge, beliefs, and values.[1] Complex decisions are more unique, which requires a thoughtful process, usually called "nonprogrammed decisions." Different authors

Figure 1. Schematic representation of steps involved in making a choice. Value-based decision making can be broken down into five basic processes: first, the construction of a representation of the decision problem, which entails identifying internal and external states as well as potential courses of action; second, the valuation of the different actions under consideration; third, the selection of one of the actions on the basis of their valuations; fourth, after implementing the decision the brain needs to measure the desirability of the outcomes that follow; and finally, the outcome evaluation is used to update the other processes to improve the quality of future decisions. Reproduced with permission.[15]



have used similar categories. For example, Dr Daniel Kahneman, Nobel prize in Economy (2002), coined the terms "system 1" (intuitive, unconscious, effortless, fast, and emotional) and "system 2" (deliberate, conscious reasoning, slow, and effortful).[17] They describe the interaction between both systems. The integration of this information, the analysis of risks, uncertainties, and alternative options, help us to make a decision according to our preferences (Figure 1).[15]

The game theory

Game theory is the study of the incentives and strategies of interactive decision making.[1,18] It provides the framework to analyze all existent strategic interactions between players.[19] The word "game" may sound trivial in an article about decision making in stroke care.[18] Actually, game strategies are not "just a game," but rather the practical application of principles for conflict resolution.

Different elements are embedded into the game theory, including: (i) players or participants, (ii) an element of risk or uncertainty, (iii) alternative ways of selecting an option (called strategy), (iv) an action (decision), and (v) the outcome (payoffs).[19] Game theory assumes that each player will try their best to reach the best payoff (preferred outcomes) according to its individual preferences. Game theory facilitates the study of cooperation and trust by evaluating the interaction between players in a specific scenario.[1,18]

Games can be classified into static (simultaneous) or dynamic (by observing the move of the opponent before deciding how to play) with complete or incomplete information (based on participants' knowledge of all other player's payoffs), one shot versus repeated, and with perfect (full knowledge of previous movements/decisions) versus imperfect (the history of the game is unknown) information. Some common examples include chess or checkers (sequential game with perfect information), auctions used in game theory (static game with incomplete information as bids occur simultaneously usually without knowing the competitor's offer).

Games are also classified based on players' interests into zero-sum games (one player's win is what the opponent losses) and non-zero-sum games (both players can win like in a trade and both players can lose like in a civil war).

Different games have been designed to identify why two rational individuals may not cooperate even when it appears in their best interest. Common to all these games, players are in the interdependence paradox of both competing and cooperating (depending on the game). An important characteristic is that each player should figure out how the other players will respond to his current move and gather information from previous moves to reach the best possible outcome. Table 1 presents elements shared by games and clinical encounters.

Medical encounters, like most of economic games and social situations in our lives are not zero-sum

Table 1. Similarities between game interactions and clinical encounters

Characteristics	Game interactions	Clinical encounters
Participants	Players	Patients or their family members
Decision to make	Yes	Yes
Information asymmetry	Possible	Commonly
Choices available	Game choices	Treatment/intervention
Strategy involved (succession of actions to reach the most desired outcome)	Yes (game strategy)	Yes (medical strategy)
Expected outcome (payoffs)	Win/loss Cooperation yes/no	Survive/dying Independence/dependency
Awareness of cross effect of their actions (the decision of cooperate may influence others)	Yes	Yes
Game paradigm (examples): **One-shot game**	Stag-hunt (single)	Acute stroke care in the ED
Repetitive-sequential	Stag-hunt (multiple)	Stroke prevention
Finite repetition	Prisoner's dilemma	Stroke rehabilitation

games. This concept means there is no single optimal strategy that is preferable to all participants, who have complementary and opposed interests.

Other situations may lead to more negative outcomes, all players losing (e.g. companies' bankruptcy or wars). Another feature is the repetition or second chances (one shot versus repeated games), interacting with the same or shifting players (e.g. sequential ultimatum game, double action). Similarly, medical encounters may occur once (e.g. emergency department, walk in clinic) or repeatedly (e.g. family doctors or group practices with different physicians under the shared patient model).[18]

Games, as well as many other activities, are governed by implicit or explicit rules. In social or political situations (e.g. passing a bill in Congress), rules are fixed, but the agenda can be managed toward the benefit of one party. Some examples of classic games are briefly summarized below (Figure 2).

The prisoners' dilemma

This is one of the most commonly used and tested experiments in game theory.[1,18] In brief, two suspects were arrested by the police for a presumed serious crime. While in jail waiting for a trial, the police questioned each of them separately and offered each a deal (a rewarding reduction in jail time if convicted) as they do not have strong evidence for a conviction. Each suspect has two options (Figure 2(a)): confess by blaming the other (also called defect) or remain silent (cooperate with the other, not to the police). Depending on each decision, there are different outcomes related to the jail time (payoffs). In this scenario, the lower the length of jail times the better for each prisoner (note: this is different from other games where larger numbers denote the preferred outcome).

If both blame (confess), they both go to jail for five years. If both remain silent, both will have a shorter time in jail. If prisoner A blame prisoner B who remains silent, then prisoner A is set free, whereas prisoner B goes to jail for 20 years (and vice versa).

Let us consider prisoner A perspective in Figure 2(a): suppose he believes prisoner B will confess, then his best option is to confess; he gets a sentence of only five years instead of 20 years (if remain silent). If prisoner A believes B will remain silent, again his best choice is to confess (he is set up free instead of a sentence of one year in jail if remain silent). In this special game (one chance for making a decision, nonrepetitive), confession for prisoner A is better than remaining silent regardless of his belief of prisoner B's choice. Therefore, the confession strategy for prisoner A is called *dominant strategy*.

Similarly, readers can analyze the perspective of prisoner B reaching the same results.

If a strategy is best for a player regardless of the others' choices, a rational player would choose it. Similarly, there are compelling reasons to believe that bad choices would be avoided no matter what other may be doing. In this game, both players have dominant strategies (confess, confess), which is the predicted outcome.

John Nash, a mathematician and Nobel prize winner, discovered an equilibrium consistent in decision makers to make a choice such that changing it would not give them a better outcome (the other player's choice remaining the same).[19] If both players have a strictly dominant strategy, the game has a unique Nash equilibrium. The unique Nash equilibrium in the prisoners' dilemma is for both suspects to confess.[20]

The dilemma then is that mutual confession (unique equilibrium) yields a bad outcome for both players. Remaining silent (mutual cooperation) is the nonequilibrium outcome that both would prefer (one year versus five years in jail); the problem is how to be certain that the other prisoner would not defect.[19]

Such cooperative behavior can be achieved in repeated plays of the game because the temporary gain from cheating (confession) can be outweighed by the long-run loss due to the breakdown of cooperation. The prisoner's dilemma is thereby characterized by a single optimal strategy and the reliance of both players on each other to achieve more favorable results.[21] It assumes a conflict between self-interest and the potential benefits achieved by cooperation. The mechanisms underlying the prisoner's dilemma are similar to those faced by many competitors, including marketers, scientists, military strategists, poker players, among others. The models used in the prisoner's dilemma offer some insights on how competitors will act to different styles of play, and these will reveal suggestions on how those competitors can be expected to react in the future.

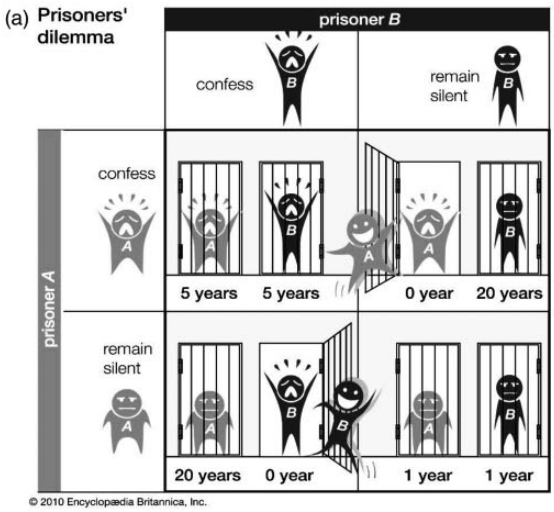
Application of prisoner's dilemma to a medical scenario

Let us consider the problem of reporting an error in administering a medication in a system with negative consequences for those held responsible. For example, a physician indicated twice the recommended tPA dose because of a weight miscalculation for a patient with an acute ischemic stroke. The pharmacist approved the high dose despite knowing the patient's weight.

How does the prisoner's dilemma predict their behavior in terms of admitting the error?

The physician and the pharmacist mimic prisoners in the game. Both are separately and simultaneously interrogated by members of the hospital board. The alternative options are to confess (blame the other) or deny (mutual cooperation). The payoffs are different

Figure 2. Common examples analyzed in game theory. *Panel a* illustrates the prisoners' dilemma (top). By courtesy of Encyclopaedia Britannica, Inc., copyright 2006; used with permission. Note that in this scenario, the lower the length of jail times the better for each prisoner. *Panel b* illustrates the prisoner's dilemma applies to a medical situation. Note that the described scenario, as well as, days of revocation of hospital privileges is hypothetical. *Panel c* illustrates the stag-hunt game. A graphical representation of the potential strategy for each hunter considering the distance to the targets. Payoff matrices for each game are in the right side.

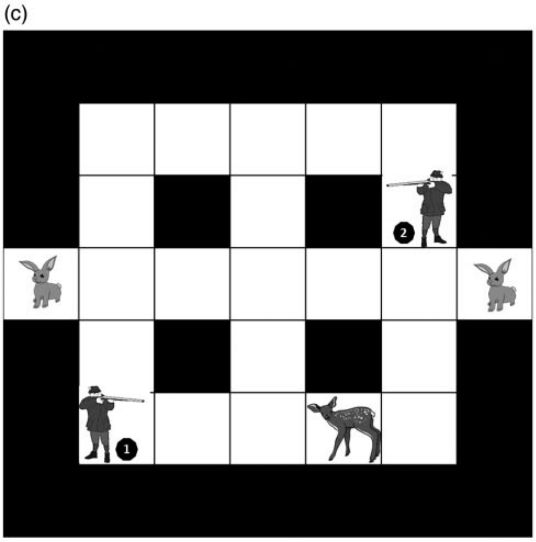


		Prisoner B	
		Confess (blame the other)	Remain silent
Prisoner A	Confess (blame other)	5 , 5	0 , 20
	Remain silent	20 , 0	1 , 1

(b)

		Pharmacist	
		Confess (blame the other)	Remain silent
Physician	Confess (blame other)	10 days, 10 days (short revocation of hospital privileges)	Free, 90 days (long revocation of hospital privileges)
	Remain silent	90 days (long revocation of hospital privileges), free	Report in physician' record, report in the pharmacist' professional record

(c)



		Hunter 2	
		Stag	Rabbit
Hunter 1	Stag	5 , 5	0 , 2
	Rabbit	2 , 0	2 , 2

degrees of consequences: short revocation of hospital privileges if both confess (the remains in their professional files), a bad report for their professional files if both remain silent. If one confess, but the other remain silent, the confessor is set up free of holding responsibility, whereas the one who remain silent will face a prolonged revocation of hospital privileges (Figure 2(b)). Although this is a real-world example, consequences (payoffs) are hypothetical as they may vary worldwide from institution to institution.

Let us analyze the physician's perspective: suppose he believes the pharmacist will confess, then his best option is to confess. He would get a short and temporary revocation of hospital privileges than a longer conviction (if remain silent). If the physician believes the pharmacist will remain silent, again his best choice is to confess (he is free of responsibility instead a short revocation of hospital privileges if remain silent). Equal rationale applies to the pharmacist's perspective (Figure 2(b)). Similar to the prisoner's dilemma game, the dominant strategy (unique Nash equilibrium) for both is to confess to avoid more severe punishments.

The dilemma for the pharmacist and the physician then is that mutual confession (unique equilibrium) yields a bad outcome for both players. Remaining silent (mutual cooperation) is the nonequilibrium outcome that both would prefer (having a bad report in their files instead of temporary revocation of hospital privileges). Again, the issue is that each provider is not certain that the other would not defect.

Under game theory, the unique Nash equilibrium is joint confession (blame the other) as both physician and pharmacist would avoid the risk of a worse outcome. Nevertheless, this scenario does not reflect a good quality of care nor reaching a desirable outcome to prevent future errors. This is one of the reason current guidelines highlight the importance of a positive reinforcement rather than punishment when disclosing medical errors (or "near misses"). Finally, this is a good illustration of why punishment for health care providers may have negative consequences for the health care system. How do we produce a system that rewards honest admissions of both parties?

The prisoner's dilemma is considered paradoxical when applied to the medical consultations. Although both patients and physicians may have their own interests, they are not competitors. A more realistic approach is a variant of the prisoner's dilemma—called the "assurance game."

The assurance game

The "assurance game" is a model of interaction involving an element of risk for each player where the best outcome is mutual cooperation.[1,18] There is no better strategy for players than cooperation if the other decides to cooperate. The classic example is the "stag-hunt" game. Two hunters can either jointly hunt a stag (an adult deer) that offers a rather large meal (higher payoff) or individually hunt a rabbit which offers a lower payoff as it is less filling. Hunting stags is quite challenging and requires mutual cooperation. If either hunts a stag alone, the chance of success is minimal. Hunting stags is most beneficial but requires a lot of trust among its members to develop a strategy to walk the field (Figure 2(c)). In this case, there are two Nash equilibria. They either both cooperate or defect (individually hunt a rabbit). The element of risk is the conditional cooperation of hunter B based on hunter A and vice versa. If the second hunter decides to defect, then the first hunter would remain hungry. There are many other examples of the benefits of mutual cooperation. In science, cooperation between investigators may lead to more productive work and novel discoveries. Other examples may involve other payers (e.g. policy-makers, stakeholders, scientific organizations, pharmaceutical companies, universities, etc.).[22] In the medical field, the stag-hunt game may offer a better representation of the interaction between patients and physicians as mutual cooperation would lead to better outcomes.

A practical example

Several years ago, one of the authors was observing a respected colleague in the stroke prevention clinic. Common for a busy Friday afternoon clinic, the last patient came back for a follow-up appointment after having had a transient ischemic attack two years ago. During the consultation, the patient mentioned he was still smoking. After providing counseling (as in previous opportunities), the neurologist told the patient that he should no longer come for a follow-up appointment if he continued smoking. Readers may find this approach of refusal to provide stroke care shocking. However, let us analyze what would be the alternatives and payoffs in this common situation by applying the game theory framework. The hunters in the hunt-stag game mimic the patient and the physician in a single or two medical visits. Cooperation would provide better outcomes for both. For example, a better payoff for the physician is the more effective investing his/her time that leads to his/her satisfaction and results in reducing the risk of cardiovascular disease. However, if the patient does not cooperate, according to game theory the best payoff for the physician would be to avoid the repetitive frustration by more effectively spending his/her time with other patient who may need that care. There are two Nash equilibriums: both patient and physician cooperate in the strategy of quitting smoking or both defect (meaning that the patient would not attempt to quit smoking and the physician will no longer follow-up the patient).[20] An interesting question is what our colleague should do when the patient clearly stated on more than one occasion that he was not interested in quitting smoking. Assuming that the patient understands and appreciates the consequences of his/her decision and knowing the substantial benefits of quitting smoking for stroke reduction (with a magnitude of effect even higher than the benefits of statins or antihypertensives),[23] physicians are trained to respectfully continue to provide care and counseling. However, according to game theory, the physician may not want to cooperate with someone who is defecting (e.g. poor investment of his time, other cooperative patients may urgently need his services).[18,20] Of course, many colleagues would argue that smoking, like substance abuse, alcoholism, or obesity, is another medical condition that requires counseling, support, and treatment. Similar situations include a bad patient–physician relationship where defection would be in the best interest of both parties. Fortunately, the sequential nature of most medical encounters through follow-up visits allow further discussion and negotiations between patients and physicians. Other sequential games that accounts for asymmetric and incomplete information (introducing medical uncertainty) may better characterize physicians' and patients' interactions. In summary, game theory provides a rationale for better understanding physicians' defection when facing uncooperative patients.

Applying game theory concepts in acute stroke care

Case scenario Part II: As seen, the best payoff for both the physician and the patient is cooperation. The patient's family inquired about the expected outcome. Is there any data to satisfy the family request? The physician cooperates by providing the requested information.

Some colleagues may provide some estimation based on the use of single variables (e.g. age, stroke severity). Others may estimate the likelihood of independence based on the availability of risk scores.[24,25] Prognostic risk stroke scores were developed in the last few years to help clinicians estimate outcomes. They differ in the variables inputted to calculate the risk of an individual.[24,25]

The treating physician facilitated some information: the patient had an iScore of 219 and a THRIVE score of 8 based on assessment in the ED. What do these numbers mean?

An iScore (www.sorcan.ca/iscore) of 219 provides an estimated probability of death within 30 days of 46% and 10–15% of independency at discharge and three months. A THRIVE (www.thrive.org) score of 8 predicts a probability of 10–15% of good outcome (mRS 0–2) at three months depending on the applied cohort. Both scores would predict a similar probability of symptomatic ICH of 15%. The physician also noted an interaction between the iScore and tPA, showing that patients with an iScore > 200 do not appear to benefit with thrombolytic therapy.[24] Moreover, the application of the iScore to three different datasets from randomized trials showed no benefits with intravenous tPA, endovascular treatment, or combined therapies in this high-risk group.[26–28]

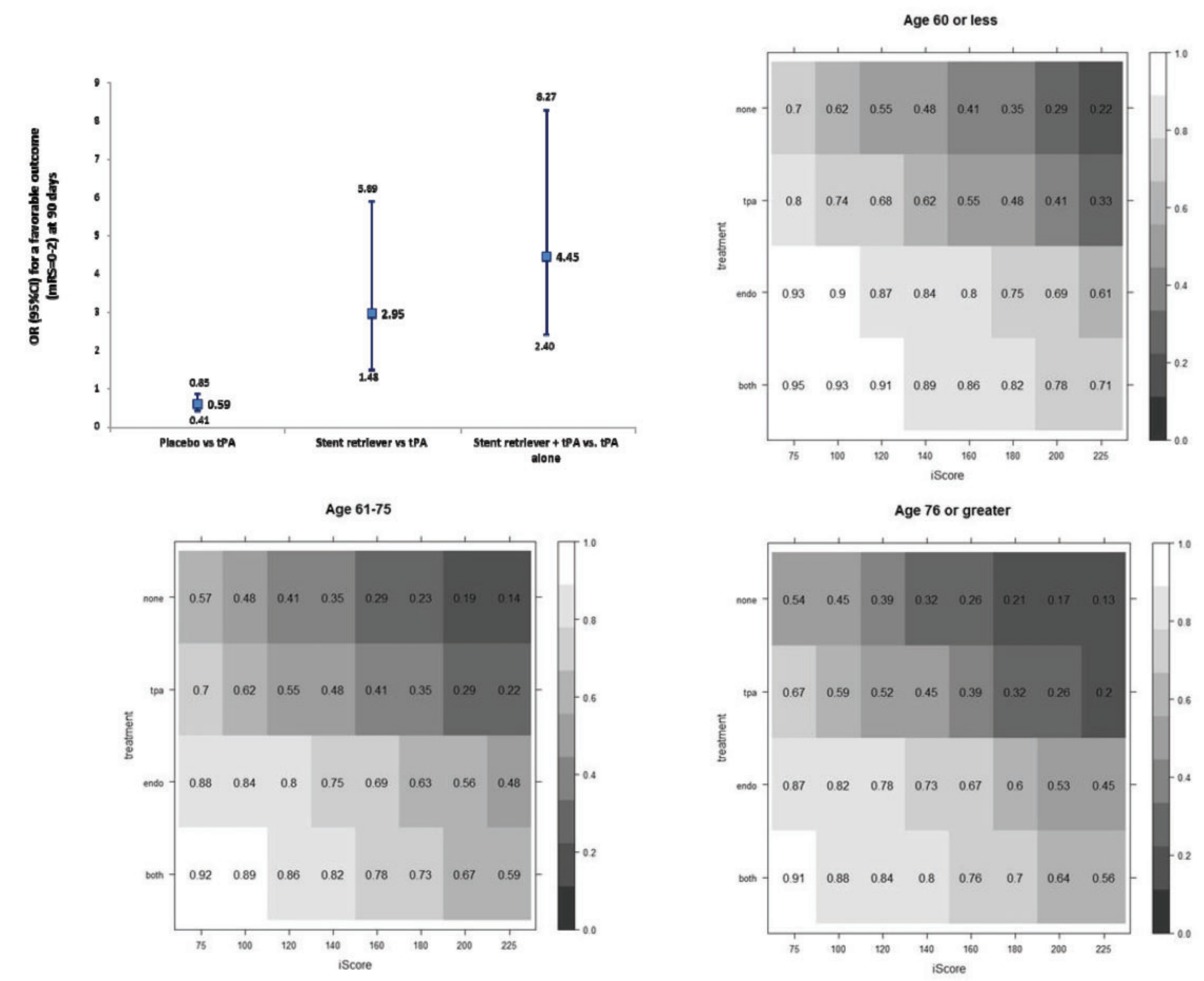
Figure 3 illustrates the probability of achieving a good outcome stratified by age, the iScore, and different interventions. Note that endovascular treatment alone or combined with tPA is the dominated strategy for individuals with lower iScores irrespective of the age (left upper and lower quadrants for each figure). The opportunity to achieving a favorable outcome for each intervention declines with higher iScores (right upper and lower quadrants), but still more aggressive interventions dominate no treatment of intravenous tPA alone.

Case scenario Part III: The family then asked what would be the physician's recommendation based on the provided information. The treating physician was uncertain about the best course considering the low probability of achieving a favorable outcome and the risk of complications (e.g. bleeding). Risk scores helped transform a situation of ambiguity (unknown risk) into a spectrum of possibilities between the risk of complications and the likelihood of achieving a favorable outcome.

Do we need more information? What are the patients' values, beliefs, and preferences?

As in the stag-hunt game, cooperation (the patient accepting the proposed treatment or the physician accepting arguments from the family against treatment) would provide better clinical and psychological (avoiding regret) payoffs for each. If the patient or family decline treatment when recommended by the physician, then they may get exposed to lower payoffs (by "missing" an opportunity to maximize the best possible outcome when rejecting the expert advice) and the negative consequences of future regret.[2] The last scenario is the physician not supporting treatment when the patient or family requests it. Then, the best possible situation for the family would be to follow the physician's advice, otherwise they would have to persuade the physician or a more difficult choice of seeking a second opinion (e.g. time consuming, availability). If they want to persuade the physician to give the treatment (physicians are not obliged to offer treatments against their will), the patient or the family may again exposed themselves to lower payoffs (worse outcome

Figure 3. Stroke outcomes according to the treatment. This figure illustrates the likelihood achieving independency (mRS = 0–2) at 90 days derived from the shift analysis adjusted for time to treatment, iSCORE, baseline ASPECT. Note greater benefits for stent retrievers alone or combined with tPA compared to tPA and no treatment (left upper panel). These findings were confirmed in recent meta-analyses published at the time of receiving the proofs.[38–41] The checkerboard graphs (WHO prediction charts) represent the probability of a favorable outcome (mRS 0–2) at 90 days by treatment modality, iScore, and age group. Numbers within each square represent the estimated probability of achieving independency (mRS 0–2 versus 3–6) at 90 days. Note: Higher probability of independence for patients receiving endovascular or combined treatment. From Saposnik et al. with permission from Neurosurgery 2015.[28]



due to treatment-related complications and regret). Note that as in the stag-hunt game, there are also two Nash equilibriums in this case scenario: physician and patients' family both accept (cooperate) or decline (defect) treatment. The alternative situations may potentially result in lower payoffs for either the family or the treating physician.

What the physician should do if he/she is against the treatment but the patient's family wants the treatment? In this situation, a nonequilibrium choice may lead to better payoffs. According to the game theory, the best outcome for the physician would be to cooperate and provide the treatment (of course, assuming there are no contraindications). Most colleagues would spend more time with the family to elaborate his/her reasons against the treatment or offer alternative options.

Game theory offers no practical solutions to ethical dilemmas (e.g. physician being asked to administer a treatment against his/her conviction). A better understanding of the patient and family's beliefs, expectations, and values would provide useful information, but also relevant learning about their perceptions which may lead to cognitive illusions.

Cognitive illusion

Case scenario Part IV: The treating physician remained thinking: "*Why do we still favor treatments for patients with high risk of complications and low probability of achieving good outcomes?*".

Most of us have been exposed to sensorial illusions. Figure 3 illustrates three common visual illusions. Most readers would perceive a larger black dot on the right while surrounded by smaller white dots, whereas the black dot on the left appears smaller while surrounded by larger white dots (Figure 4(a)). Similar distortions can be appreciated for the length of lines (Figure 4, panels b and c). However, a ruler can prove that the lengths are equal.

Cognitive illusions or perception distortions are more difficult to prove.[29] Studies showed a change in decisions when a third less preferable alternative is added. For example, Dan Ariely—a behavioral economist—conducted an experiment after observing an advertisement in *The Economist*.[30] One hundred students were presented with three options: an online subscription for $59, a print subscription for $125 (less preferable) or the combo option (both online and print subscription) for $125. Overall, 84% of students choose the combo option and 16% the online subscription. When participants were presented with only two options (the print subscription that nobody wanted was removed), then results were surprisingly reversed (68% choose the online subscription alone).[30] The explanation is based on a change in the reference point in the first offer (the combo being perceived a better deal) that was different in the second (a one-to-one price comparison of two similar options) had a significant impact on the students' decisions.[17] A similar effect was shown in other domains (e.g. the challenging task of choosing health insurance, purchasing goods). In other words, when we compare different options, we use reference points. A third or fourth alternative may act as a "distractor" (even when it appears irrational or is an option that nobody would choose) creating the *cognitive illusion* that the first or second options have greater value.[29] This distractor creates an asymmetric dominance or distortion effect (also called decoy bias) also explaining other common observations in human psychology (e.g. the introduction of a medium quality but highly priced third jacket would help increasing the sales of a better quality, but more expensive one compared to the sales when two extreme options are available).

When physicians face a critical decision in acute stroke care, there may be several alternatives. As illustrated before, either intravenous tPA or endovascular treatment appears even better options when no acute treatment (the option that most would not choose) is also on the table. The recent positive results of the stent retriever trials (ESCAPE: OR for a favorable outcome 2.6; 95%CI 1.7–3.8; MR CLEAN OR 1.67; 95%CI 1.21–2.30) introduce new challenges by modifying our cognitive perceptions.[31,32] For example, tPA may be perceived as a "middle option" and also appear less preferable when compared to the benefits of stent retrievers.[28,31,32] This is also illustrated in Figure 3, where the probability of achieving a favorable outcome is significantly better by using stent retrievers alone or combined with intravenous tPA compared to tPA alone or no treatment.[28] Physicians are also prone to the optimistic bias and illusion of control, thus leaning toward being more proactive than remaining passive in critical situations.[29] Together, the reference point and the optimistic bias may explain our perception that some treatments appear the most appealing option even in scenarios with marginal (if any) benefit (e.g. probability of independence).

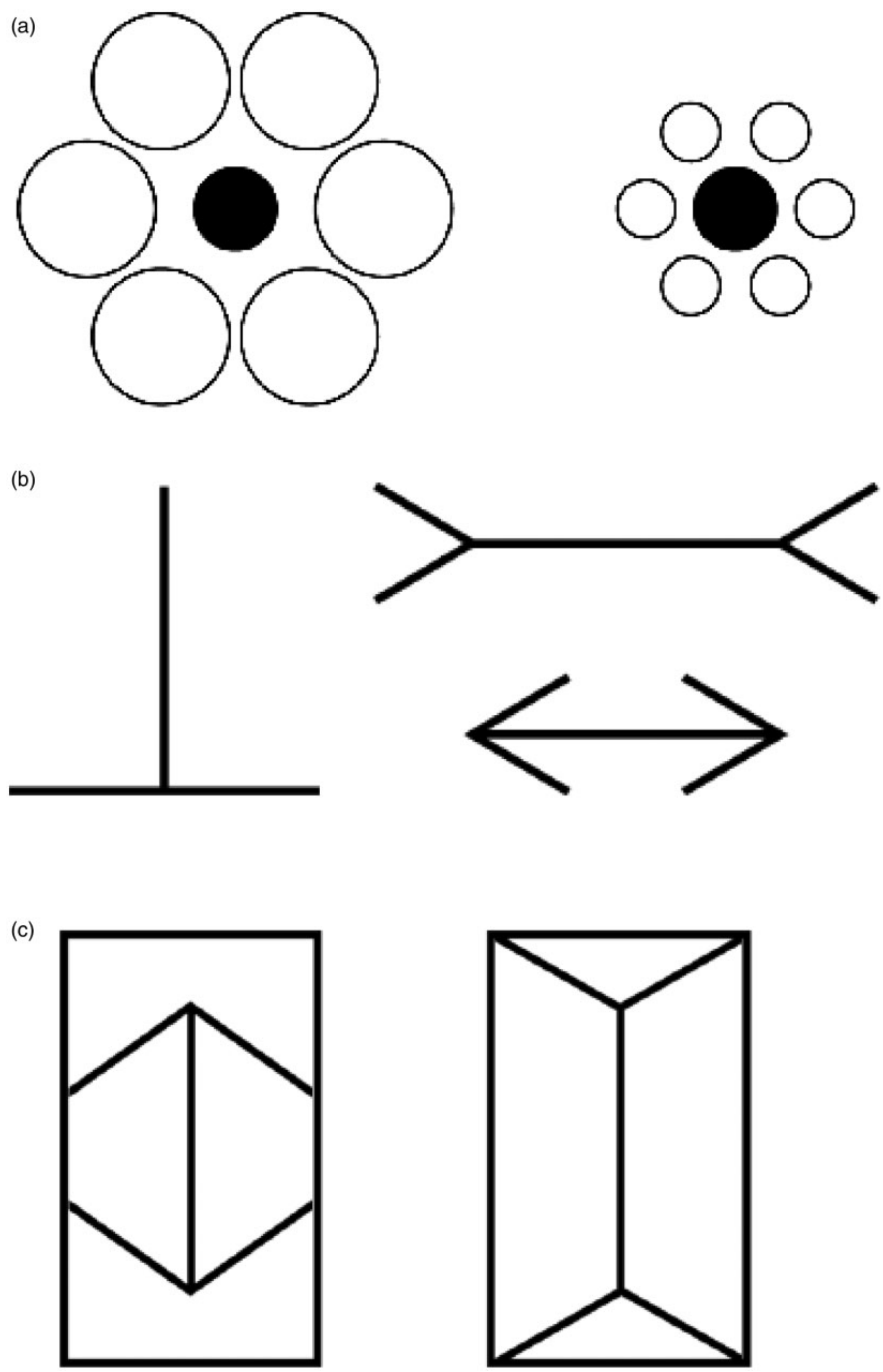
Rethinking outcomes

What is the goal of a competitive game? Most people would answer "to win." Others would respond "to have fun." What is the goal of any medical encounter? Several answers may coexist, including gaining patients' trust, offering high quality of care, achieving a positive outcome, or more importantly helping patients feel better.[33]

However, the magnitude of the "victory" counts in competitive games, markets, and patients care. In game theory, the number associated with the "victory outcome" is determined by the payoff. The underlying assumption is that individuals try to maximize the payoff, which depends on our internal value and representation system (the value we assign to goods, health states, etc). Knowing your own values and beliefs, calculating the risk in a particular situation, understanding our and the other "player's" risk tolerance and our ability to defer a discussion for a better time (e.g. temporal discounting in stroke prevention) would offer a better stance. Game theory can be applied to enhance our understanding of medical encounters with limited compliance to treatments or the lack of patients' cooperation for suggested investigations. Two examples include: the understanding of families' beliefs while counseling about endovascular treatment in a high-risk scenario and the strategy of deferring the discussion to the next closer appointment for a reluctant patient with a cryptogenic stroke undergoing invasive investigations (e.g. transesophageal echocardiogram and a conventional angiogram).

Previous studies suggest physicians may not account for patients' preferences when providing recommendations or making diagnostic or therapeutic decisions.[34] Consequently, those decisions are made on physicians' beliefs and preferences, which are the result of previous experiences (historical records encoded in our brains). Depending on the nature of past outcomes and the

Figure 4. Visual illusions. This figure illustrates the appearance of one object compared to another depending on accompanying elements. The black dot on the right appears larger when surrounded by smaller white dots, whereas the black dot on the left appears smaller when surrounded by larger white dots (Figure 3(a)). The lengths of the lines are equal (panel b). The length of vertical lines within the rectangles is also equal despite the larger appearance of the right one in the context of open arrows (panel c). A ruler can demonstrate equal lengths.



current clinical situation, we unconsciously compute prediction errors: the probability of achieving independence in that particular patient with stroke based on our previous learning (e.g. own observations and reading from the literature).[1,35] The diversity of stroke presentations and underlying mechanisms lead to a wide variability of exposures and outcomes. Cognitive biases and the complex interaction of factors influencing stroke prognosis may affect our clinical judgment when making crucial decisions.

Paraphrasing Charles de Gaulle, are we bringing solutions or are we part of the problem?

The aim of this article was to: (i) offer a different perspective on the treatment of acute stroke by learning from the game theory, (ii) apply strategies to improve our interactions with patients and their families, (iii) increase awareness of situations of the challenges of nonequilibrium choices (e.g. prisoners' dilemma), and (iv) the need of having a better understanding of our patients' and families' beliefs, preferences, and perceptions. Ultimately, we all aim for the best possible outcome following expert advice under uncertainty.[3,36]

Take-home messages

Acute stroke care represents a challenge for decision makers. What can we learn from decision neuroscience, game theory, and the aforementioned case scenarios?

1. Decisions under constrains: In acute care, we have to make decisions in a short period of time, with imperfect information, evaluating the most appropriate therapeutic options while learning about patients and families' values, preferences, and beliefs.
2. Internal and external factors influence our decisions: Physicians are exposed to the challenges of multitasking in the ER (e.g. making simultaneous decisions about other patients) which may predispose to medical errors.[37] Increasing awareness and limiting interruptions in emergency care would ameliorate the risk of erroneous decisions.
3. Most situations faced by emergency practitioners, clinicians, and neurologists may be straightforward falling under "system 1" (intuitive, repetitive, programmed decisions). Our challenge is to be aware of more complex situations to be good team players in nonprogrammed decisions (system 2). Game theory brings some strategies to help us manage complex medical situations under uncertainty.
4. Considering alternatives: therapeutic decisions are commonly based on the application of results from randomized trials, guideline recommendations, etc. However, game theory offers a different perspective by encouraging the consideration of different alternatives by understanding others and the careful evaluation of "distractors" when applying "real–world" data.
5. Cooperation and trust: The hunt-stag game teaches us the importance of trust to strength cooperation for a successful patient–physician interaction that is beyond a good or poor clinical outcome.
6. Action plan: Further studies combining medical scenarios and experiments commonly used in decision neuroscience may identify the impact of cognitive distortions (e.g. tolerance to risk, overconfidence, illusion of control) on medical decisions. Moreover, specific studies using classic games with imperfect information applied to stroke care would provide a better understanding of physicians' response in complex situations (e.g. one-time short ER encounters, families demanding unsuitable treatments) leading to more satisfactory patient–physician interactions.

Authors' contribution

We declare that we have participated in the conception, design, analysis, interpretation of results, drafting the manuscript, and made critical revisions of the manuscript.

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