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Original article

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Neuroeconomic models: applications in psychiatry

Summary

Neuroeconomics is a discipline aimed at investigating the neural substrate of decision-making using, along an interdisciplinary way, research methods and information deriving from economics, cognitive and social psychology, and neuroscience. The combination of economic game theory and neuroscience has the potential to better describe the interactions of social, psychological and neural factors that may underlie mental illnesses. These concepts will allow a description of psychopathological disorders as deviation from optimal functioning. Neuroeconomic models can lead to identify quantitative phenotypes that will allow for further investigations in individuals with mental disorders. In this paper evidences from the interaction between neuroeconomics and psychiatry are reported, supporting the utility of economic concepts such as under ambiguity/risk and social decision making to psychiatric research, in order to improve diagnostic classification and therapy eventually.

Key words:
Neuroeconomics • Decision making • Game theory • Psychiatric disorders • Social cognition • Social decision-making

Introduction

In October 2017 Richard Thaler was awarded with the Nobel Prize for Economics for its contribution in integrating the economic and psychological analysis of the individual decision-making process. This award has sealed, if ever there was a need, the importance of the neuroeconomics, as a relevant field of interest in which economists as well as psychologists and psychiatrists focused their studies. The aim of neuroeconomics is the understanding of human decision making (DM) using, along an interdisciplinary way, research methods and information deriving from economics, cognitive and social psychology, neuroscience.

Alterations of DM processes have been studied not only in the human 'behaviour', investigating how neuroeconomic models, i.e. the study of how the economic behaviour can drive the person to do "the best for himself" and the best way to utilize resources, but also in psychiatric disorders.

Neuroeconomy and decision making

The neuroeconomic perspective focuses and explain the needs derived from adaptation and survival. Deployment and utilization of the resources in order to obtain the maximum reward and the best probability of survival is an economical question eventually. This perspective possesses therefore an evolutionary computational connotation in terms of adapting energy expenditure in the environmental economy so that the probability of survival can be maximized. Although it could seem complex, everyone in its everyday life operates decisions, quite automatically, without apparent mental effort.

DM implies complex processes involving higher-order cognitive functions, as executive functions are, focused to the choice and regulation of the

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possible action that lead to the optimal outcomes. It modulates reward and punishment perception so that advantageous choices can be made.

DM processing by the central nervous system depends from three temporally and functionally distinct, although partially, processes: assessment and formation of preferences among the possible options; selection and execution of an action; experience or evaluation of an outcome [1].

Being DM so pervasive and necessary for human, both in physiological and in pathological cognition such as in mental disorders, necessity to obtain information to understand choice mechanisms and their link to neurobiological substrates is warranted. To do so, application of game theoretic probes (i.e. economic games) as quantitative ways to investigate subjects' choices that match or deviate from optimal has been productive.

Economic games, far from being an object of amusement, are approaches to understand the features of strategic interactions, a decision problem with structure, so that the player's payoffs can depend on its motivated choices under some input. These games reflect the investment of the limited energetic resources of an organism to pursue prey or food resource in the presence of uncertainty: choices therefore that are of biological value under selective pressure. They permit to explore the limitations in capacity to estimate probabilities, calculate the likelihoods of payoffs and the risks involved, and, as the game progresses, the player capacity to adequate its behaviour.

Several research paradigms have been elaborated to investigate and compute these real-life DM processes, likely the most utilized is the Iowa Gambling Task (IGT) [2]. It was developed for the evaluation of the orbitofrontal cortex (OFC) functioning associated with uncertainty, reward, and punishment processing.

This task permits to investigate the degree to which a subject selects small immediate gains, but associated with long-term gains (advantageous option), over large immediate gains associated with long-term losses (disadvantageous option). It also measures two kinds of decisions under uncertainty, i.e. risk and ambiguity. Decisions under ambiguity have to be performed in the first trials, while choice under risk in the last trials of the task as the game progresses.

The distinction between these two kind of uncertainty is based on the probabilities assigned to the outcomes. A choice under risk is linked to a foreseeable probability of possible outcomes and their associated payoffs, i.e. the player has some possibility to estimate the probability of the outcome. A choice under ambiguity instead possesses little or no evidence for having confidence in the assignment, with the unclear possibility to forecast the outcome. Evaluation of sensitivity to risk and ambiguity is important in the investigation of cognitive processing of persons with mental disorders for which impulsivity valuation and the DM can be perturbed [3]. The risky condition, in which an outcome probability prediction could be reliably estimated is more frequent in everyday life. However, the outcome of choices under ambiguity is inevitable and necessary eventually, to compute the risk of future decisions based on probability knowledge.

Recent studies using gambling games reported abnormal DM performance in several mental disorders. From a clinical perspective, this impairment can be considered a transnosographic trait that may influence the therapeutic response, determinate interpersonal difficulties, be related to suicidal risk and aggressive acts. It can be a feature of a wide range of *impulsive spectrum* disorders. The personality trait of impulsivity has been frequently suggested to be associated with DM impairment: subjects with impulse control problems display a decreased reasoning on the consequences of their choices. This can be the case, for instance, of disorders such as addiction and schizophrenia [4].

Estimation of the impulsivity often expressed by addicts, utilized DM games in order to determinate temporal discounting behaviours. Drug addicts by definition make poor decisions, such as continued drug abuse in the face of adverse consequences (i.e. a kind of 'myopia for the future'); gambling tasks can identify quantifiable neurobehavioural hallmark of addiction. Persons with alcohol dependence have been found to operate more disadvantageous choices leading to lower scores in their IGT performance, significantly related to impulsivity evaluation. These data suggest that DM impairment is related to impulsive dimension, an important feature in subjects with alcohol dependence likely with a role in increasing the proneness to a chronic relapsing course [5 6].

Studies using DM games, particularly IGT, on patients with schizophrenia showed conflicting results. Some of these did not find differences from healthy controls [7], while other ones showed instead impairment [8]. Researches examining the association between DM performance and symptoms of schizophrenia suggest that OFC dysfunction is associated with social behaviour impairment and possibly negative symptoms [9]. Moreover, imaging studies examining neural correlates of IGT revealed that subcortical areas, other than OFC, were highly involved in DM processing [10]. These subcortical areas can be associated with different symptoms. Some studies reported a positive association between IGT impairment and negative symptoms [9], although an association with positive symptomatology was also found [11]. Interestingly, recent reports show that individuals with schizophrenia are particularly impaired during the last IGT trials [11 12]. As a matter of fact, after an initial strategy in facing choices under ambiguity similar to that of controls, patients did not modify their DM behaviour when the choices are under risk, operating disadvantageous choices because they continue their behaviour as they cannot forecast probabilities.

Motivational difficulties might have further accentuated the differences in DM performance [13]. These observations support a problematic lack of shifting behaviour using DM strategies that may lead the subjects to poor functioning suggesting this impairment as a relevant cognitive underpinning of functional outcomes.

The capacity of neuroeconomic games to capture real life DM, possessing highly recognized ecological validity more than most laboratory tasks, leads them to be suitable instruments to explore the relationship between decision making and community functioning outcomes [14]. This association has been found in both in individuals with a substance abuse diagnosis [15] and subjects with schizophrenia [16].

These observations could support the hypothesis of dopamine (DA) as a *wind blowing* on the decision making impairment [17]. If so DA can be considered as a key neural substrate for tracking the value of stimuli and actions and modulating decision-making within a neuroeconomic perspective. DA abnormalities have been implicated in regulation of energy expenditure, characteristic across disorders, such addiction and schizophrenia, as well as depression and attention-deficit hyperactivity disorder, all showing a common dysfunction in the brain allocation of energy and resources in economic DM.

Social decision making

The human brain is essentially 'designed' to be social [18]. If so the social exchange and interactions necessitate the capacity to assign or refuse credit for shared outcomes in order to act appropriately. In social exchanges, computation of assignment of credit for an outcome is essential. Breakdown of assignment of social agency is a feature of several mental illnesses such as schizophrenia and autism spectrum disorders. Social agency computations are the basic models of other's mental states comprehension, i.e. the so called theory-of-mind [19,20].

The gap between decision-making in real life, where the influences of the social context are relevant, and the decision-making process evaluated in the laboratory often intentionally without any social influences, is wide.

The combination of Game Theory tasks with the neuroeconomic paradigms in the study of social DM, can allow greater understanding on how decisions are made in an interactive environment. This is the case of the games of bargaining and competition, in which the brain system of reward and the ability in the strategic game is linked to the evaluations of the intentions of the other [21]. In other words, the thoughts and actions of an 'agent' depend on the variation of the actions and mental states of other social 'agents' [22].

Decision making in complex social interactions needs to interpret intentions and the development of a Theory of the Mind (ToM) of others; this capacity is mediated by the medial prefrontal cortex function [23]. An extended neural network contributes to the evaluation of the costs and benefits of social and socioeconomic exchange of the decision-making process, including cooperation and altruistic punishment.

The literature on game theory can provide guidance on solving problems related to social exchange. The cooperation and sanctioning of non-cooperative behaviour (i.e. the altruistic punishment) is regulated by cognitive and emotional mechanisms that have evolved in human beings in response to the need for mutual cooperation in complex social groups. The ToM, the prediction of reward, and the appreciation of social norms, are necessary, although sometimes not sufficient, mechanisms involved in social exchange and functioning.

Economic exchange games represent a relevant quantitative research paradigm to evaluate the social exchange, in terms of the subject's internal norms assessment for the fairness in an exchange, and they require that each subject models their partner's mental state.

There are several games, computationally well-defined, widely used as experimental probes in social DM research: the most known are the prisoner's dilemma, the dictator game, the ultimatum game, the trust game. These games have been proven valuable in clinical populations.

The most known and used is likely the 'ultimatum game' that offers a good example to the comprehension of cooperation or altruistic punishment behaviours. It can be also defined as a game 'take-it-or-leave-it': it involves two players, a proposer and a responder. The proposer possesses a given resource, e.g. 100 euros, that have to split with a responder. For instance, the proposer offers 20 euros to the responder, maintaining for itself the remaining budget. If the responder accepts the split, both 'take' the money, otherwise neither one gets anything (i.e. 'leave'). Theoretically the proposer should give the minimum possible to the responder, while this latter should accept all non-zero offers. This is not instead the case, where the modal offer is 40/100 and in 50% of the cases the responders refuse the 80/20 split proposal. This is a behaviour observed across different cultural and experimental settings and provides the detection of the usual response to fairness deviations [24].

This is however a so called 'one-shot game', a kind of game that does not provide the possibility of observing the result of the social signal offered to the partner, as well as the response, i.e. the consequent learning. The

social signal is indeed devoted to the expectation of adjusting the future partner's behaviour in the interaction.
This opportunity can be seen in games involving cooperation by repeated interactions (relationships) with possibility to modulate the relationship in a more ecological setting, such as by multi-round fairness games.
Neuroeconomic paradigm using this approach is the iterated 'Trust Game'. Similarly to the ultimatum Game it is based on a shared sense of fairness that lead to a mutually satisfying exchange [25]. The 'player' has the role of 'investor' that send some money to a social partner, the 'trustee'. The sum sent arrives automatically tripled to the 'trustee' that has the possibility to choose the sum to repay the 'investor'. *Trust* can be therefore quantified as the amount of money one person sends to the other one. If both players in this game share and act upon a common social norm, for example they share the winnings of a game equally, an optimal shared strategy is used: e.g. the 'investor' sends its entire endowment to the social partner and this 'trustee' sends back half of the tripled investment. If so, a shared norm and cooperative strategy mutually benefit both players. If the investor instead considers the payment from the trustee too poor, he can refuse it and both the players don't receive nothing.
Again, as in 'one shot' game, the 'investor' should accept all non-zero offers, giving instead the 'trustee' the minimum possible. Differently from this basic theory, the modal observed behaviours show a rejection of less than 20% of the total amount, showing a tendency to altruistic punishment that con modulate the subsequent responses to fairer exchanges. The game therefore is really based on trust: if the 'investor' and the 'trustee' respect trust reciprocating money, both players end up with higher payoff.
These neuroeconomic quantitative/computational paradigms have been used to study social interaction in mental disorders, such as borderline personality disorder (BPD), externalizing behaviour problems, depression, social anxiety, psychosis [26].
Studies of BPD with iterated Trust task showed failure in cooperation, associated with an insensitivity of anterior insular cortex [27 28]. In a study on adolescents with externalizing behaviour problems a reduced reciprocity during social reasoning independent from ToM functioning was shown [29]. Monterosso et al. [30] provided similar evidences in the addiction area. Ernst [31] examined reward-related and goal-directed processing in relation to symptoms of depression supporting connection of the DM processing to neural dysfunction. Diminished activity for social than to non-social partners (i.e. a computer) in a region of the medial prefrontal cortex implicated in ToM was found in patients with social anxiety. Patients with psychosis showed lower baseline levels of trust compared to healthy controls at Trust Game [32].
These results demonstrated a validity of neuroeconomics tasks to investigate and discriminate psychiatric disorders.

Future directions

Although the social neuroeconomic tasks used are of relatively good ecological value, they present however some pitfalls. As a matter of fact, the conceptualization of 'social cognition' is limited because these tests are typically 'off-line', i.e. are related to hypothetical scenarios in which the participants 'do not interact' and the event does not happen in real time, does not represent a real social interaction, does not elicit full emotional and behavioural involvement.
An alternative paradigm is the integration of a computer-aided task by which the subject experience a real social neuroeconomic interaction, i.e. the interchange is 'on line' with a 'Trustee' that responds in real time to the investment proposal of the subject. The subject, moreover knows some essential characteristics of the partner, such as name, sex, age (Fig. 1). Preliminary data using this paradigm show association of the neuroeconomic indexes, such as invested and gained money with daily life functionality (Riccardi et al., in preparation).

Conclusions

These studies suggest that fairness games through the neuroeconomic computations they provide can identify quantitative phenotypes in individuals with mental disorders.
Social exchange is common to all humans. When the biological substrates implementing these models are damaged or altered, abnormal behaviour is expressed. Economic games are beginning to provide new ways to capture and quantify this behaviour and the associated neural correlates, and may produce new biomarkers of mental diseases [33].
DM impairment can be considered a transnosographic trait that influences the symptomatology of many disorders and modulates the therapeutic response. Its definition allows a reformulation of those conditions that are described with various terms such as "impulsivity", "disinhibition" and "risk taking behaviour". All these generic descriptive terms can be interpreted in the light of knowledge about DM processes; their evaluation can offer useful information in the psychopathological, clinical and rehabilitation fields.
DM processes, particularly those relating to decisions under risk conditions, are associated with the functional deficit and social cognition constructs in people with mental disorders, such as schizophrenia.
The study of the diagnostic and predictive utility of neuroeconomic approaches in understanding these conditions is at the moment at the beginning. The possibility however that the DM processing investigated by fair-

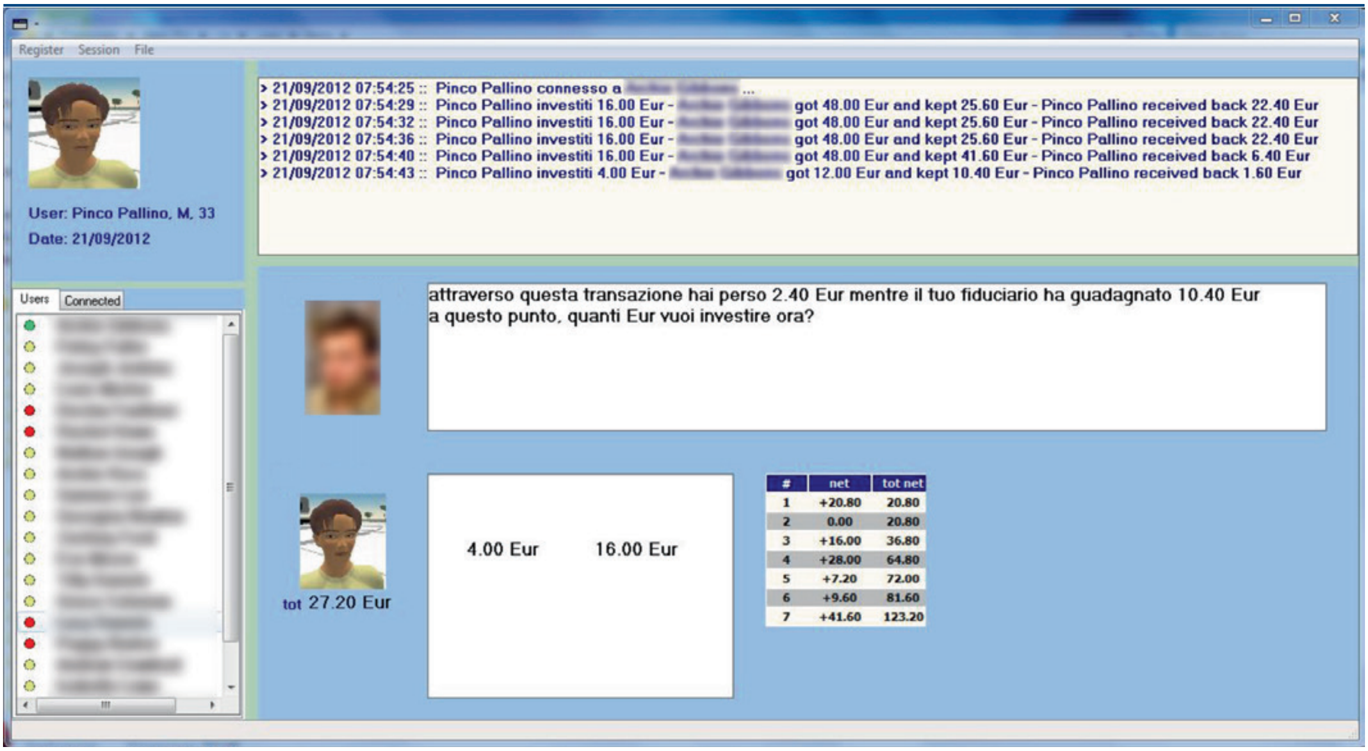

FIGURE 1. *Trust game 'on line': example of an ongoing economic transaction.*

ness games could be sensible to modulation by pharmacological (e.g. serotonergic or oxytocin modulation) or other kind of interventions (e.g. cognitive remediation) is exiting [4].

Once that the concept of DM will reach an adequate definition in pathophysiological, neuropsychological and neurochemical terms, there will be real possibilities for the elaboration of a rational intervention for people presenting such clinical manifestations.

Conflict of Interest

None.

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