Presidential Address

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Welcome to the 60th Anniversary of the Western Neurosurgical Society. It has been a great honor to be President of this august society for the past year. To me, the Western is about people, and I have greatly enjoyed getting to know many of my neurosurgical colleagues and their families since I joined the Society in the 1980's. One of the pleasures of serving as your President is the privilege of presenting the Presidential Address.

Neuroeconomics is a fascinating subject that uses neuroscience to investigate how we choose and how we make decisions. It is a combination of economics, psychology and neuroscience. It is about acquiring rewards and avoiding losses. Neuroeconomics is about learning, choice under risk and ambiguity, delayed gratification, the roles of emotions in decision-making, and strategic and social decisions.

Neuroeconomics: Benefit

Neuroeconomics generates models which can predict economic and social behaviors, grounded in neurobiology. With an understanding of neuroeconomics, economists will be able to answer: Why do two individuals faced with the same information and incentives make different choices? Why does the same individual sometimes make choices that are inconsistent? Furthermore, understanding variation in choices is fundamental to effective public policy.

Neuroeconomics: Chess Analogy

Neuroeconomics is like chess. Imagine a chess tournament with round one involving two economists playing on a standard chess board. Round two pits the winning economist against a psychologist on a two-layered chess board. Round three is analogous to the essence of neuroeconomics where a economist and psychologist compete with a neuroscientist on a three-layered chess board.

Round 1: Two economists, Samuelson v Friedman

During the first round, two neoclassical economists, Paul Samuelson and Milton Friedman, line up to compete, black vs. white respectively, on a standard 64 square board. Samuelson's chess reputation is based on his fundamental representational theory of economics. Friedman's chess reputation is based on expected utility theory. Samuelson's game reflects his economic theory that choosers show the common regularity of consistency due to the fact that they harbor a single internal representation of the unique values of their options. In other words, the key feature of Samuelson's game is that **choice** "reveals" a subject's underlying preferences. Simple: we know his preferences based on his choices. Friedman's game on the other hand focuses on the importance of bounded theory, a soft theory of economics, which argues that models made predictions only *as if* the equations they described were computed. Once again, simple: we can predict his moves as if he were following a computational chess strategy. The chess game begins and we see both players following the neoclassical economic rules of the game. Samuelson and Friedman reveal their preferences and each attempts to predict the future behavior of the other. It is apparent to the crowd observing the game, that neither Samuelson nor Friedman has goals, hopes, or desires. Their preferences are the proximal causes of their behavior. **Checkmate.** Friedman prevails utilizing the simplest possible theory to guide his game. The crowd politely applauds, and a challenger steps forward.

Round 2: Economist v psychologist

The second round of the tournament pits the neoclassical economist against a psychologist. The officials bring in a new chessboard with two layers, each with 64 squares. The psychologist states that chess is a much more complex game that transcends the concept that observed choices or actions can be used to infer preferences. The psychologist's chess game involves the experience of his choices in moves as choices of mental states and choices about happiness. The crowd eagerly waits to see whether the economist's preferences can hold up to the psychologist's attempt to maximize his happiness. **Stalemate.** The economist and psychologist shake hands, acknowledging their equality in the game. But who should play in the third round of the tournament? Given the synergies and overlapping of their game theories, they decide that they would **both** play.

Round 3: Economist and psychologist v neuroscientist

Enter the third round opponent, a neuroscientist. The crowd of observers starts to whisper, then becomes more vociferous about the possibility of such a match: economist and psychologist versus a neuroscientist? What would be the purpose? What could possibly be the outcome? The crowd further reacts when the chessboard is wheeled in to the tournament room: a 3-D board. Star Trek fans immediately recognize it as the Tri-Dimensional Chessboard. Choices and utility of moves are going to be analyzed by the competitors according to economics and psychology, but what would be added by neuroscience? The neuroscientist explains that his moves will be based on ultimate causes rather than proximal causes or happiness. He states that successful moves improve his ability to reproduce. The crowd snickers thus he expounds further, explaining that chess moves are analogous to actions we make on an every day basis that help us survive and reproduce. These actions are often performed without any conscious awareness and are a product of the behavior-generating areas of our brains. A chess move is no longer just a move. Each move is a product of evolutionary biology, able to be analyzed and explained by the complicated and highly modular nature of our brains.

The neuroscientist makes it clear that the championship chess match will be representative of a global theory involving economics, psychology and neuroscience and will involve human decision making explained with mathematical theorems predicted with behavioral analysis, and mapped in the brain. The crowd remains hushed throughout the match which lasts days, as the historical 3-D chess game pushes the frontier of the "Theory of Knowledge" with novel consilience and reductive synthesis.

This time it is clear that one of the competitors is disadvantaged in the endgame given a subtle but apparent lack of clarity as to how to handle some of the most complex of the 3-D moves. The neuroscientist admittedly notes that he was stymied several times by not seeing many moves into the future. Also when certain moves were made, the precise circuitry linking the moves was not elucidated. He requests that the game be replayed with each competitor in an functional MRI machine. The judges of the chess tournament of course deny this request. Nevertheless, the neuroscientist is able to achieve a stalemate. The naysayers in the crowd doubt the value of such a three way game. But the competitors recognize the inherent value in their historic game. The economist, psychologist, and neuroscientist learn from each other and proclaim that 3-D chess best represents the fundamentals of each of their respective fields. Further, they recognize that they had created a new multidisciplinary field, neuroeconomics, which will help in the understanding and explanation of human decision making. The neuroscientist proposes that the chess tournament no longer be sponsored by the Chess Foundation, but instead should become a collaborative venture between the social sciences and natural sciences, sponsored by the Foundation of Neuroeconomic Analysis.

Neuroeconomics

Let's relook at the definition of neuroeconomics: it is the use of neuroscientific measurement techniques to investigate how decisions are made. It's about acquiring rewards and avoiding losses. It's about learning. Neuroeconomics is about choice under risk and ambiguity, delayed gratification, the role of emotions in decision-making, strategic and social decision. Here is an example of applied neuroeconomics: whether to accept a job as a Goldman Sachs analyst for $100k/yr with few future pay increases or advancement vs a job as a stockbroker at $40k/yr with the potential for much greater income if successful, but the risk of being fired if not.

Homomorphisms

Neuroeconomics is able to apply neuroscientific principles to economic behavior, often via psychology, using reductive linkages called homomorphisms. Homomorphic reductions exist between economics and psychology, psychology and neuroscience, and economics and neuroscience. Let us now define these three elements which form neuroeconomics.

Economics

Economics is defined as the science which characterizes the optimal allocation of scarce resources. In essence, this is decision-making, which is equivalent to CHOICE. Economics models individuals valuing rewards and choosing among alternatives. Decision-making involves measurable tasks: obtaining information from the environment regarding possible actions, valuing those actions, and choosing between them. There is a hierarchy of how decision are made: determining one's objective(s), filtering incoming information, accessing memories of related events, using heuristics (experienced-based techniques for problem solving), and identifying constraints on cognitive processing.

Psychology

Psychology is defined as how physical stimuli give rise to a subjective experience called a percept. Classical psychophysics is a mathematical subset of psychology which utilizes signal detection theory. There are two key features of psychophysics: first, the relationship between stimulus and percept has been reductively linked to neurobiology models of sensory or stimulus transduction and encoded by the brain. Second, these psychology-neuroscience linkages are linked to the economic concept of utility.

Neuroscience

The sensory and motor systems are the two key functional elements of the brain as it relates to the choice mechanism. The sensory system can be viewed as a three-step process: transduction, encoding and initial processing, and cortical processing. Transduction is the conversion of extrinsic stimuli to neuronal action potentials. The visual system can be utilized to illustrate the three-step process, as this neurological function has been studied and mapped in great detail. The external sensory stimuli are topographically organized in the brain. The motor system functions in a similar topographically organized fashion. Neuroscientists believe that there is likely neural evidence for the following: subjective value, probability, expected subjective value, and a "neuro-computational mechanism" that interacts with the motor system to produce action that reflects choice. The sensory and motor organization of the brain allows the neuroeconomist to specify a theory of choice that can be linked to expected utility theory. The nervous system can be modeled to make predictions about behavior, and the neural structures that underlie choice behavior can be linked to utility theory. John Maynard Smith, a 20th-century theoretical evolutionary biologist is quoted as implying that evolutionary forces including natural selection are examples of the effects of a utility-based economic overlay to our nervous system.

Economics: Choice

Samuelson proved that choice and utility were identical. The basis of modern neoclassical economics is that if you choose A over B, you cannot also prefer B over A. More of a good thing is better than less of a good thing. A stronger theory is that choosers can never be satiated, and a chooser behaves as if he/she had internal utility functions. However, from the neurobiological perspective, choice and utility are really separate and distinct. Utility is linked to subjective value, and subjective value leads to action. This is the theory of expected utility – <u>the foundation of neuroeconomics.</u> Choosers who obey the axioms of expected utility should be treated as if they multiply the utility of each object by the probability of obtaining that object to yield an expected utility for each option in their choice set, and as if they select the option having the highest expected utility. <u>Utility implies welfare.</u>

Foundation of Neuroeconomics: Expected Utility

Expected utility is projected onto neuronal firing rates. These neurons fire at rates in a valuation circuit in the brain which encodes subjective values of each of the objects being chosen. Values are proportional to behavioral measurements of the expected utilities of these objects. The end result is that individual choices have unique utility functions which are mapped to neurobiological function with subjective values.

Neuroeconomics: Goals

This brings us to the goals of neuroeconomics:

- Identify the location in the brain where these subjective values are encoded
- Clearly discern <u>economics</u> at the <u>neural</u> level
- Understand the <u>neural basis</u> of <u>risk aversion vs risk seeking</u>
- Best describe <u>choice</u>
- Build models that <u>predict human behavior</u>
- The focus is on proximate causes of behavior and how psychologies affect decisions.
    - Laws are more effective and precise when proximate rather than ultimate causes of human behavior are known

Neuroscience

Subjective value is encoded in the lateral interparietal area (LIP) in a way that predicts later action. This neurological linkage is analogous to the way the mathematical equation called "argmax" links utility and choice. The "argmax" operation is an economics concept that asserts that choosers always pick the best of their options. This is a "Hard" economic concept with significant implication for neuroeconomics. The "Hard" theory requires that there be brain circuitry for subjective value and that the brain be able to implement an argmax operation, or in pure economic terms, a reservation-price-based decision. The brain does perform these operations. Because of this, "Hard" economic utility is not the basis of choice behavior, but rather "Hard" random expected utility is the preferred theory. Neurobiological studies have shown that all neural signals including expected subjective value are stochastic, or random. Thus one is asking the same question regarding neuroeconomic stochasticity when you pose the following two homologous questions: "How, neurobiologically, is the inter-neuronal correlation adjusted by other brain circuits?" and "How, economically, is the slope of the stochastic choice function adjusted as choice conditions change?" To sum up the analogy between the analyses of choice from the economics perspective and the neurobiological perspective respectively we have the following neuroeconomics mapping algorithm:

Expected utility → Reservation Price → Price → Choice to Expected Subjective Value → Threshold → Action

The critical point is that neurobiologic stochasticity and economic stochasticity can be linked. This iterative process reductively links neuroscience, psychology, and economics, and maximizes predictive power. These reductive linkages are shown in this diagram.

Valuation

After establishing the principles of the neuroeconomics multidisciplinary approach to choice, I will now describe the neuroeconomics approach to the process of valuation. In neoclassical economics, choice is value, but in modern economics, value transcends choice. Let us discuss marginal utility and its neurobiologic correlates. The nervous system depends on reference points to encode external stimuli and most importantly, objective values of consumable rewards are not encoded. In fact, the brain does not ever encode the objective properties of anything much less our primary rewards. The brain encodes various properties of outside stimuli in reference to a drifting baseline, i.e., either above or below a drifting reference point, using a transforming function. In economics terms, this is the question of "how good" or in other words, marginal utility. Objective value is never encoded in our brains, which poses a problem: if we accept this reference-based subjective sensation theory, then we must incorporate into neuroeconomics theory that people really do behave irrationally. As irrational behavior does occur, neuroscience tells us that "Hard" economic theory may indeed not be accurate, and that the fundamental structure of our brain leads to some irrational choice. Neuroscientific research has demonstrated that our actions are guided by reference-based subjectivizations of sensory input and much of our memory, which is relevant to choice theory. Neuroeconomics must adjust to the fact that the reference point for value does vary, but this is where evolutionary biology comes into the picture. These "irrationalities arise because evolution is trading off the costs of accurate sensory encoding against the costs of irrational decision making." The neural reference mechanism increases the encoding systems of sensation and memory, and the cost of this increased efficiency is "violations of rationality under some conditions."

The neurophysiology of circuits associated with dopamine and valuation forms the basis of neuroeconomic theory of valuation that begins with cell membranes and extends to utility theory. There is neurocircuitry in which dopamine is the agonist in learning and valuation. One of the key points is that dopamine neurons encode a prediction error from which the expected value of an action can be computed. Another basic point is that synapses are modified by experience. The neural circuits involving dopamine give rise to a subjective value-encoding scheme; from the psychological perspective, these circuits involve near-normative learned representations of value; and from the economic perspective, the circuits are related to "reference-dependent computations that seem to underlie human choice."

The expected subjective values of actions are located in the frontal cortex and striatum. These regions are connected with the amygdala and insular cortex, which are the center of valuation. fMRI studies have proved that the medial pre-frontal cortex and the striatum are the likely regions where value is encoded, and that the orbito-frontal cortex provides a key input to the central valuation areas in the medial pre-frontal cortex and striatum. The amygdala was also found to convey more negative than positive information about value to the orbito-frontal cortex and striatum. The precise circuitry is unknown, and that the precise way value is constructed and "options are selected for arbitration in the choice circuits" is also unknown.

Major Research Topics in Neuroeconomics

The major research topics in neuroeconomics include reward acquisition, certain ambiguity and delayed gratification, learning and strategy and cooperation. I will briefly elucidate each of these research topics.

Reward Acquisition

Research in reward acquisition has shown that gains or "neural rewards" are located in the right hemisphere, particularly in the hypothalamus and nucleus accumbens. On the other hand, losses are located in the left hemisphere, particularly in the amygdala. Losses, which are emotional responses, are associated with fear or regret – a phenomenon based in the amygdala. Anticipation of rewards is based in the dopamine-receptor-rich ventral striatum. Notification that a reward was earned is functionally based in the mesial prefrontal cortex.

Certain Ambiguity and Gratification Delay

The major research topics related to certain ambiguity and gratification delay have proven that:

- Most people are ambiguity averse
- Ambiguity studies have produced ambiguous results as to activation of brain regions
- There is a unique ability to postpone current gratification for a later, larger reward
- There is strong desire for current reward and rapid devaluation of future rewards

- The choice of immediate vs delayed gratification is a battle between limbic structures (current reward) and neo-cortical regions (evaluate trade-offs)

Learning and Strategy

The major research topics related to learning and strategy include:

- Neural basis of learning including
    - Neurotransmitter glutamate
    - Long-term potentiation (LTP)
    - Strengthening of connections between neurons
- Reinforcement learning, located in the amygdala and orbito-frontal cortex
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Cooperation

The final major research topic in neuroeconomics is cooperation.

- Ability to cooperate has positive and negative neural reinforcers
    - The positive reinforcer is a reward, located in the striatum
        - Requires attention
        - Conflict: making more money but being less socially acceptable
        - Emotional component
        - Strongest activation is somatosensory association cortex (posterior parietal) linking experienced emotions with decisions
    - The negative reinforce is the loss of a larger reward and neural activity due to social condemnation
- Theory of mind (model of the other person's mind)
    - Medial orbitofrontal cortex
- Binary trust game (iterated prisoners dilemma)
    - Both parties gain by cooperating, but cannot coordinate cooperation, thus both choose to be non-cooperative
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Cooperation (cont'd)

A fascinating study was performed by Sanfey, who used an fMRI during an ultimatum game. The major findings were consequences of not cooperating. When first decision makers (DM1s) offer less than 30% of the money, the second decision makers (DM2s) nearly always reject the offers, which is irrational from an economics point of view. The DM2s felt angry when DM1 was stingy. Unfair offers activated the insula, dorsolateral prefrontal cortex, and cingulate. Insular activation is associated with disgust, pain, hunger, and thirst. Sanfey's conclusion: low offers are rejected because of disgust.

Another study showed that interpersonal trust is the most powerful predictor of whether nations will have rising standards of living. Further, the study showed that the neuroactive hormone oxytocin processes signals of trust and induces trustworthy behavior.

In a Trust game, DM2s receiving trust signals had 2x normal oxytocin levels. High progesterone levels signified less trustworthiness because progesterone inhibits oxytocin uptake. Oxytocin activates parasympathetic system and facilitates dopamine release, and is physiological motivator of cooperation.

Value of Neuroeconomics

The value of neuroeconomics is a synthesis of principles from economics, psychology, and neurosciences:

…consider the choices humans and animals make when they sample probabilistic rewards repeatedly, when they learn the value of an action through experience. Traditional neoclassical economic theory employs the axiomatic notion of expected utility to explain these kinds of choice. That theory fails because the independence axiom is violated. Traditional psychological theory proposes that an iterative learning process produces an associative strength related to the notion of utility but is silent on choice. Neurobiological studies of dopamine-based systems describe, in molecular detail, the process by which synaptic strengths are changed by rewards and connect those synapses to movement production via structures in the fronto-parietal networks.

Only the combination of economics, psychology and neuroscience can provide a complete model of choice and decision making. Reductive linkages or consilience among the three disciplines has bridged the gap between social and natural sciences and will provide answers to the following huge unsolved problems in neuroeconomics:

1. Where is subjective value stored and how does it get to choice?
2. Who says when it is time to choose?
3. What is the neural mechanism of complementarity?
4. How does symbolic probability work?
5. How do state and utility function interact?
6. What is the neural organ for representing money?

These six questions represent the present limitations of neuroeconomics, but there are normative issues which may even be more important to recognize. Neuroeconomics is essentially a theory of expected subjective value and there could be profound implications for normative theory if we further develop the ability to measure expected subjective value in the human brain.

Conclusion

In 1898, Thorstein Veblen stated: "Economics properly understood, is simply a branch of biology."

Humans survive and <u>reproduce</u>. This requires that <u>choices</u> be made to acquire resources, value alternatives and choose among them. Resource acquisition requires interaction with others, sometimes strategically.

<u>Neuroeconomics provides a way to measure neurophysiological activity during the process of choice.</u>

My personal conclusion is best described in Goethe's "Faust":

- *I've studied now Philosophy,*
  And Jurisprudence, Medicine,
  And even, alas, Theology:
  From end to end, with labor keen;
  And here, poor fool! With all my lore
  I stand, no wiser than before;
  I'm Magister-yea, Doctor-high,
  And straight or cross-wise, wrong or right,
  These ten years long, with many woes,
  I've led my students by the nose,
  And see, that nothing can be known!

And to further clarify the relationship of economics, psychology, and neuroscience, here is The Brain as explained by John Cleese….

Reference: **<u>Foundations of Neuroeconomic Analysis</u>,** by Paul W. Glimcher