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Aging and Neuroeconomics: Insights from Research on Neuromodulation of Reward-based Decision Making

Abstract: 'Neuroeconomics' can be broadly defined as the research of how the brain interacts with the environment to make decisions that are functional given individual and contextual constraints. Deciphering such brain-environment transactions requires mechanistic understandings of the neurobiological processes that implement value-dependent decision making. To this end, a common empirical approach is to investigate neural mechanisms of reward-based decision making. Flexible updating of choices and associated expected outcomes in ways that are adaptive for a given task (or a given set of tasks) at hand relies on dynamic neurochemical tuning of the brain's functional circuitries involved in the representation of tasks, goals and reward prediction. Empirical evidence as well as computational theories indicate that various neurotransmitter systems (e.g., dopamine, norepinephrine, and serotonin) play important roles in reward-based decision making. In light of the apparent aging-related decline in various aspects of the dopaminergic system as well as the effects of neuromodulation on reward-related processes, this article focuses selectively on the literature that highlights the triadic relations between dopaminergic modulation, reward-based decision making, and aging. Directions for future research on aging and neuroeconomoics are discussed.

0. Introduction

Neuroeconomics is a new field of interdisciplinary research that emerged around the turn of the 21ˢᵗ century. It calls for new conceptual, theoretical, as well as methodological developments in combining cognitive neuroscience, computational neuroscience, psychology, and behavioral economics to investigate *in vivo* the brain processes involved when individuals make economically relevant decisions (e.g., Camerer/Loewenstein/Perlec 2005; Fehr/Fischbacher/Kosfeld 2003; Glimcher 2003; Glimcher/Rustichini 2004, Platt/Glimcher 1999; Sanfey/Loewenstein/McClure/Cohen 2006; Zak 2004). From the perspective of neuroscience, this new interdisciplinary endeavor opens up possibilities to tap into the neural basis of decision processes that more closely match the daily economic contexts individuals encounter. This can be achieved by using normative models from decision science (e.g., the expected utility model of von Neumann/Morgenstern 1944) and economics (e.g., the risk value and the related portfolio selection theory by Markowitz 1952) as well as modern experimental paradigms from behavioral and experimental economics (Camerer/Loewenstein/Rabin 2003; Kagel/

Roth 1995) to help probe into the cross-level interactive mechanisms of economic decision making on the behavioral and neuronal levels. From the perspectives of behavioral economics, neuroeconomics is a modern attempt to understand the micro, individual-based processes of preferences and choice behavior that interact with the macro, society-based economical processes that set the contexts of individual economic decisions. Historically, this has been the research agenda advocated by the classical economist Adam Smith (1759) since the 18th century. In this regard, recent advancements in non-invasive brain imaging techniques and computational neuroscience methodologies provide means to get at neurobiological mechanisms that shed light on micro processes of economic models.

Modern economic theory has its origin in Pascal's theory of expected value (1623-1662; 1948). Pascal argued that the expected value of any course of action could be determined by multiplying the actual magnitude of a gain (x) that can be realized from that action with the probability (p) of receiving that gain. It is then considered that individuals make their choices by evaluating the expected values of different possible courses of actions. Pascal's framework, however, does not take into account the individual's subjective preferences and falls short in predicting choice behavior in conditions involving risk or uncertainty, for instance. Bernoulli (1738; 1954) modified Pascal's theory of expected value by also considering the individual's subjective desirability of a choice, which often involves a transformation of the objective gain. The transformation reflects properties intrinsic to the decision maker, such as his/her current wealth, risk preferences, or their interactions. Formally, power functions are most commonly used for transforming expected values into expected utilities.

Contemporary models of financial decision making also try to formally tackle 'risk' associated with decision. For instance, the risk-value models are based on the assumption that investors select among financial alternatives by trading off risk and expected value (Sarin/Weber 1993). The most prominent of these models is the 'expected return—variance of return' rule, which uses the variance of the expected return as a parameter of risk. Based on this rule, it is proposed that, at a given value of expected return, individuals minimize risk by choosing the portfolio of one or several investments that has the smallest variance (Portfolio Theory; Markowitz 1952). In this context, other than objective measures of risk, such as the variance of expected values (or expected returns), the individual's subjective perception of risk often need to be taken into account as well in order to predict economic behavior (e.g. Klos et al. 2005).

1. Examples of Formal Decision Parameters at the Neuronal and Cortical Level

Animal studies using invasive electrophysiological recording techniques as well as human studies using non-invasive neuroimaging methods have revealed neural correlates of key parameters specified in economic theories. These include the magnitude of a desired outcome as well as the probability, uncertainty, or risk associated with it.

Studies of perceptual decision making with rhesus monkeys (e.g., Kim/Shadlen 1999; Janssen/Shadlen 2005) have established the involvement of neurons in the lateral intraparietal (LIP) area in reflecting properties of the visual stimuli (e.g., the quality of sensory inputs and temporal integration of visual signals). Integrating paradigms of perceptual decision making with reward based learning, Platt and Glimcher (1999) showed that firing rates of the animal's LIP neurons during simple perceptual decision making could be sensitive to the magnitude and probability of the expected gain (e.g., reward in terms of drops of fruit juice). In a two-choice cued 'lottery' paradigm, the expected gain magnitude (e.g., from 0.25 to 0.75 ml of juice) and the probability (from 0.2 to 0.8) of reward were independently manipulated across blocks of trials. Both expected gain magnitude and gain probability modulated the firing rate of LIP neurons (see Fig. 1 panels A and B, respectively). The averaged firing rates across trials also showed functional relations to the two key parameters of expected value (see Fig. 1 panels C and D, respectively). Moreover, the firing rate of the neurons further reflects the combined effects of reward magnitude and probability independent of these two components, very much as the theory of expected value would predict. In a similar vein, other animal studies on neuromodulation of reward processing showed that midbrain dopamine neurons could rapidly adapt to the information provided by reward-predicting stimuli, such as reward magnitude, probability, and uncertainty (see details in the section on neuromodulation of reward processing).

In research with humans, a range of functional neuroimaging studies provides evidence for distinct functional brain circuitries that are sensitive to reward magnitude, probability, and uncertainty. For instance, Critchley et al. (2001) found that, during an anticipatory delay period, brain activations in anterior cingulate and orbitofrontal cortices are modulated by outcome uncertainty, though uncertainty (or risk) in this case was defined synonymously as probability. Similarly, Volz et al. (2003) varied winning probabilities systematically and found correlations with activations in the frontomedian cortex (BA8), the anterior insula, the middle frontal gyrus, and also in the anterior cingulate cortex. In a follow-up study Volz et al. (2004) identified the frontomedian cortex as the common cortical substrate mediating uncertainty, independent of whether the cause of uncertainty was external (i.e., the probabilistic decision outcome) or internal (the deterministic decision outcome not yet learned by the individual). Building on these findings Preuschoff et al. (2006) designed a task that allows not only the investigation of reward probability, but also reward variance, which is commonly assumed to be an objective measure of risk in economic theories (Sarin/Weber 1993). In contrast to the findings of Volz et al. (2003, 2004), Preuschoff et al. found that reward variance modulates activations in bilateral insula and bilateral ventral striatum. Based on these results, one could conclude that risk is at least partly represented by the brain's reward system. This conclusion is in line with findings from another study (Kuhnen/Knutson 2005), which showed that activity in the nucleus accumbens (part of the ventral striatum) preceded risky choices. In addition, Kuhnen and Knutson (2005) found correlations between the degree of uncertainty involved in the decision and activation in the anterior
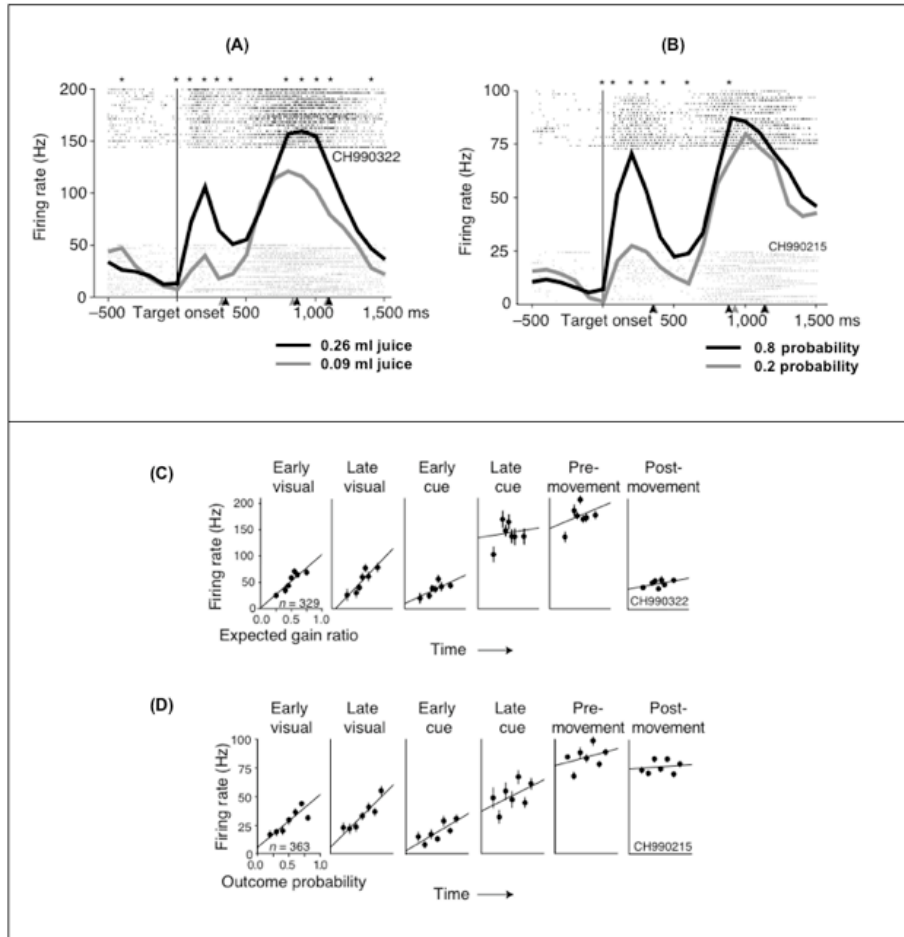
Figure 1: (A) Firing rate of neurons in the lateral intraparietal area is sensitive to reward amount and (B) reward probability. (C) (D) Furthermore, average firing rate across trials also show functional relations with these two parameters of expected value. (Adapted with permission from Platt & Glimcher, Copyright Nature, 1999).

cingulate cortex. So it seems that risk-relevant information is, at least in part, processed by the anterior cingulate cortex and its interactions with brain regions implicated in reward processing (e.g., striatum). Using an associative-learning paradigm, a recent study also investigated the functional brain circuitries that are sensitive to parameters of expected value (magnitude and probability) and uncertainty (Tobler/O'Doherty/Dolan/Schultz 2007). In line with earlier findings, activation in the striatum was modulated by expected rewards, but with finer sensitivity compared to earlier results obtained from simpler tasks: Stimuli

associated with higher expected values elicited monotonically increasing fMRI responses in the striatum, independent of different combinations of magnitude and probability. A distinct representation of reward magnitude was identified in the striatum and the medial and lateral prefrontal cortex, and for reward probability also in the striatum and in the orbitofrontal cortex. Furthermore, stimuli associated with higher uncertainty (i.e., higher variance) elicited greater activation in the lateral orbitofrontal cortex. In a similar vain, Knutson et al. (2005) examined related phenomena in a monetary incentive delay task and reported representations of expected gain magnitude in the nucleus accumbens, of expected gain probability in the medial prefrontal cortex, and of expected value in both, striatum and medial prefrontal cortex.

Taken together, the above findings from invasive electrophysiological recording studies in animals and non-invasive neuroimaging studies in humans showed that micro processes implementing the various decision parameters as specified in economic theories can be traced out both at the level of single neuron electrophysiology and at the level of functional brain circuitries. Note, however, that in many of these studies (e.g., Tobler et al. 2007; Knutson et al. 2005) participants did not actually have to choose between a range of options. Therefore, further neuroeconomic research will need to use experimental designs that include broader sets of choice options in order to show how these basic decision parameters are further processed in the brain to reach decisions across different contexts. Although extant evidence indicates that neuronal and cortical mechanisms can implement the basic decision parameters that are specified by the theories of expected value and expected utility, it would be erroneous to conclude that decision behavior is predominantly biologically driven and devoid of contextual influences. Alternative theories that emphasize contextual factors and their effects on decision strategies should be considered, too. For example, even though people can form representations of risk and value of choice options, they do not always trade off these attributes as predicted by risk-value models when composing investment portfolios as exemplified by the home country bias (Huberman 2001). Instead, people seem to be heavily influenced by the characteristics of decision environments, for instance the composition of available investments (Benartzi/Thaler 2001; Rieskamp 2006). More generally, neuroeconomic research will generate further insight into (economic) decision making and underlying neuronal processes, if it considers the interaction of decision maker and decision environment (e.g., Hutchinson/Gigerenzer 2005), and compares how alternative models can account for decision processes (see, e.g., Hampton et al. 2006).

2. Neuromodulation of Reward-based Decision Making

Brain mechanisms both at the system and at the neuronal level are delicately modulated by their neurochemical contexts. Evidence accumulated to date indicates that various transmitter systems (i.e., dopamine, norepinephrine, and serotonin) affect processes of economic decision making. For instance, it has been proposed that norepinephrine is implicated in regulating choice behavior for

optimizing task-related outcome on both shorter and longer timescales (Aston-Jones/Cohen 2005). Genetic polymorphisms of serotonin transporter genes have been found to affect probabilistic learning and more general cognitive control functions (Chamberlain/Muller/Robbins/Sahakian 2006; Roiser/Rogers/Cook/Sahakian 2006). In addition to these unitary effects, behavior and cognition are most likely modulated by complex interactions between these transmitter systems (e.g., Benaliouad/Kapur/Rompre 2007; Chamberlain et al. 2006). Below we focus our review, however, on dopaminergic modulation mainly because current evidence on aging-related decline in the dopaminergic system as well as evidence on dopaminergic modulation of reward processing are better consolidated.

Fifty years ago dopamine (the amine 3-hydroxytyramine) was first identified as an independent transmitter, other than being the precursors of noradrenaline and adrenaline (Carlsson et al. 1957; Montagu 1957). In subsequent decades, much research progress has advanced the understanding of the distributions of dopamine neurons (see Björklund/Dunnett 2007 for review) and their functional effects on motor (see Cenci, 2007 for review), cognitive (Goldman-Rakic/Muly/Williams 2002; Seamans/Yang 2004 for reviews), reward-related mechanisms (Schultz, 2007 for review) and motivational functions (Berridge 2007; Wise 2004 for reviews), as well as more general functions of optimal behavioral and cognitive control (see Aston-Jones/Cohen 2005; Graybiel 2005; Montague/King-Casas/Cohen 2006).

2.1 Midbrain Dopamine Neurons and Decision Parameters

Of specific interest here is dopamine's involvement in reward-based decision making. Evidence from animal single neuron recording studies show that about 75% of midbrain dopamine neurons (e.g., located in the substantia nigra and ventral tegmental area) show transient, phasic activations following primary food or liquid rewards and reward-predicting (i.e., conditioned) stimuli (i.e., CS). Specifically, dopamine neurons' responses to reward seems to code prediction discrepancy bidirectionally, such that once a reward-predicting stimulus is conditioned (i.e., CS), a reward amount exactly as expected following the CS would elicit no response; whereas, an unexpected larger amount of reward (positive-predictive discrepancy) would elicit an activation and the omission of the expected reward would induce a depression of firing activity (see Figure 2A; Schultz et al. 1997; Schultz 2002 for reviews). Furthermore, more recent studies also showed that activations of midbrain dopamine neurons signal reward prediction in a rather fine-tuned manner corresponding to key parameters of classical economic theories. For instance, the activation of dopamine neurons functionally reflects the expected value of a reward independent of the combinations of reward probability and magnitude (Fig 2B top panel; Tobler/Fiorillo/Schultz 2005). Further, there is evidence showing that reward-induced phasic activations of dopamine neurons also vary monotonically with the extent of uncertainty (Fig 2B bottom panel; Fiorillo/Tobler/Schultz 2003), whereby uncertainty is greatest when

probability is 0.5 and smallest when probabilities are at the extremes, either 1.0 or 0.0. The midbrain dopamine neurons project in a general topographic order to the striatum, ventral striatum, and most areas of the neocortex, particularly, the prefrontal cortex including the anterior cingulate (Björklund/Dunnett 2007). Therefore, dopamine's role in signaling reward prediction can flexibly interact with other aspects of cognitive functions, such as prefrontal attentional regulation and executive control processes, to guide adaptive behavior.
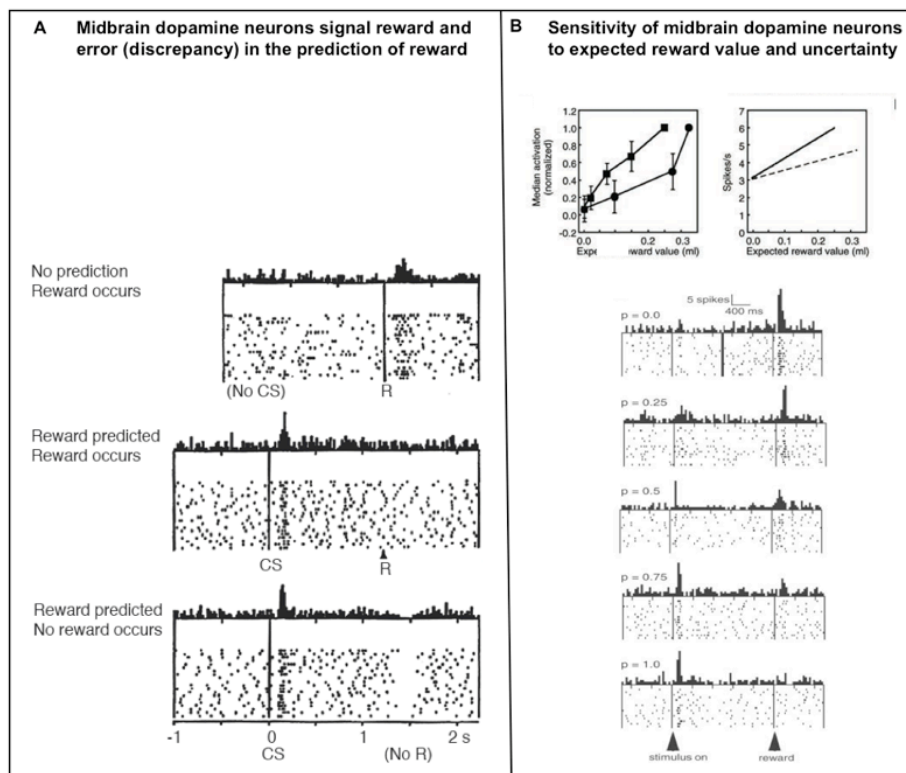

Figure 2: (A) Activations of midbrain dopamine neuron signal reward prediction (adapted with permission from Schultz et al., 1997, Copyright *Science*, 1997). (B) Sensitivity of midbrain dopamine neurons to expected reward value and uncertainty (adapted with permission from Tobler et al. and Fiorillo et al., Copyright *Science*, 2005, 2003 respectively).

2.2 Modeling Neuromodulatory Gain Control of Reward-based Decisions

Since the early theoretical work by Friston et al. (1994), a range of neurocomputational approaches has been taken to explicate the functional roles of neu-

romodulation as a powerful mean to implement value-dependent modulation in the brain to guide adaptive goal-directed behavior and decision making. Different approaches differ with respect to implementation details (e.g., mimicking Rescorla-Wagner law based Pavlovian conditioning or Hebbian predictive learning based on temporal differences in rewards). The models also differ with respect to their conceptual emphasis on incentive salience (e.g., Berridge/Robinson 1998) or discrepancies in reward predictions (e.g., Montague/Person/Dayan/Sejnowski, 1995; Sutton 1988; Dayan/Abbott 2001).

Varieties in implementations and conceptual emphasis notwithstanding, in general dopaminergic signaling of reward can be modeled as a quantity (commonly denoted as δ_t) that reflects the mismatch (difference or discrepancy) between the expected reward based on learning history and the actual reward obtained. The relation between dopamine's role in reward prediction and goal-directed action can be formally modeled, and two levels of influences have been suggested in one common framework (McClure/Daw/Montague 2003). At the level of reward processing, dopamine first indirectly influence decision making in a learning context by influencing the strength of the reward prediction discrepancy (δ_t) in temporal difference models. At the level of choice behavior, the strength of dopamine modulated prediction discrepancy can then be directly linked to choice selection by relating choice probability with the prediction discrepancy in the sigmoidal (logistic) activation function. Specifically, choice probabilities are functionally related to the perceived difference between reward options (δ_t) that are successively considered for choice. The slope of the sigmoidal function scales the sensitivity of choice probability with respect to reward prediction. The greater the slope the more choice behavior is sensitive to variations in rewards. This scaling parameter in principle can be varied to account for individual differences in the efficacy of dopaminergic modulation that are either related to aging (see Bäckman et al., 2006 for review) or to relevant genetic polymorphisms, such as the catechol-O-methyltransferase (COMT), dopamine receptor, and transporter genes.

3. Aging and Dopaminergic Modulation: Empirical Evidence and Computational Models

Over the past two decades, studies investigating the impact of aging on the brain's neurochemical processes have yielded consensual evidence to show that the efficacy of various neurotransmitter systems declines. Of particular interest here are aging-related declines in different aspects of the dopaminergic system (Bäckman et al. 2006; Marschner et al. 2005), given its involvement in reward-related decision making. Declines in dopaminergic function are present both with respect to presynaptic dopamine transporter (DAT) mechanisms as well as postsynaptic receptor binding mechanisms. For instance, using PET and a D2-like receptor ligand it has been demonstrated that the efficacy of postsynaptic receptor binding declines during aging (Kassinen/Rinne 2002; Figure 3A). Similarly, age-related decrease in DAT density in the caudate and the putamen was

shown in a recent PET study on dopamine and cognitive aging (Erixon-Lindroth et al. 2005, see Figure 3B). In terms of the extent of decline, two recent studies (Kassinen et al. 2000; Inoue et al. 2001) show that, on average, there is about 10% decline in receptor binding efficacy across a variety of brain regions, including the regions involved in reward-processing (e.g., prefrontal cortex and limbic regions).
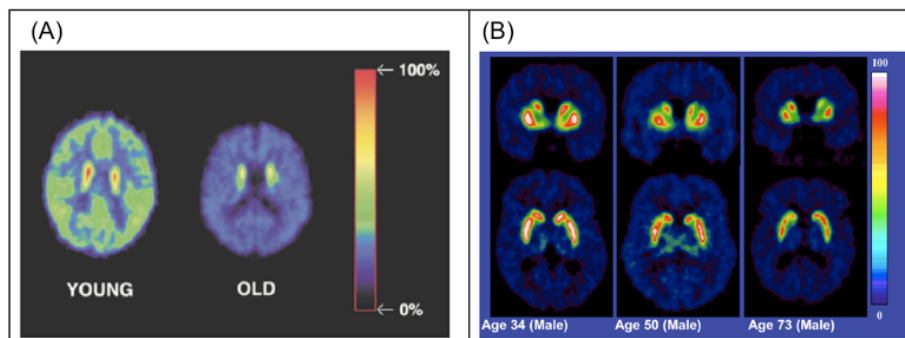

Figure 3: (A) Aging-related reduced D2 receptor binding efficacy in caudate nucleus as seen in PET (adapted with permission from Kaasinen & Rinne, Copyright Elsevier, 2002). (B) Declines of DAT density in caudate putanmen as a function of age (adapted from Erixon-Lindroth et al., Copyright Elsevier 2005).

Various neurocomputational models have been proposed to link aging-related decline in dopaminergic neuromodulation to behaviorally observed cognitive deficits. One of these models relates weakened phasic activity of the mesencephalic dopamine system with aging-related deficits in detecting performance error (Nieuwenhuis et al. 2002). Another model focuses on capturing the effect of deficient dopaminergic neuromodulation on compromised prefrontal cortex functions, such as cognitive control (Braver et al. 2001). A third model captures the effects of deficient neuromodulation on processing variability and the distinctiveness of memory and goal representations in more general terms (Li et al. 2001). Specifically, this model captures aging-related decline in dopaminergic neuromodulation by stochastically attenuating the gain control (G) of the sigmoidal activation function that models presynaptic to postsynaptic input-response transfer (Fig. 4A).

With large inputs, a direct consequence of reducing the slope of the sigmoidal activation function is increased within-network random activation (Fig. 4B). This, in turn, leads to increased performance variability in simulated aging networks with attenuated G (Fig. 4C). In contrast, if G is increased to excessive values, the activation function becomes a step function and activation variability depends critically on the amplitudes of inputs. Activation variability is markedly reduced with large positive or negative inputs, and increased with intermediate inputs. These properties of stochastic G tuning predict an inverted-U function (Fig. 4D,E) between the levels of dopaminergic neuromodulation, distinctiveness
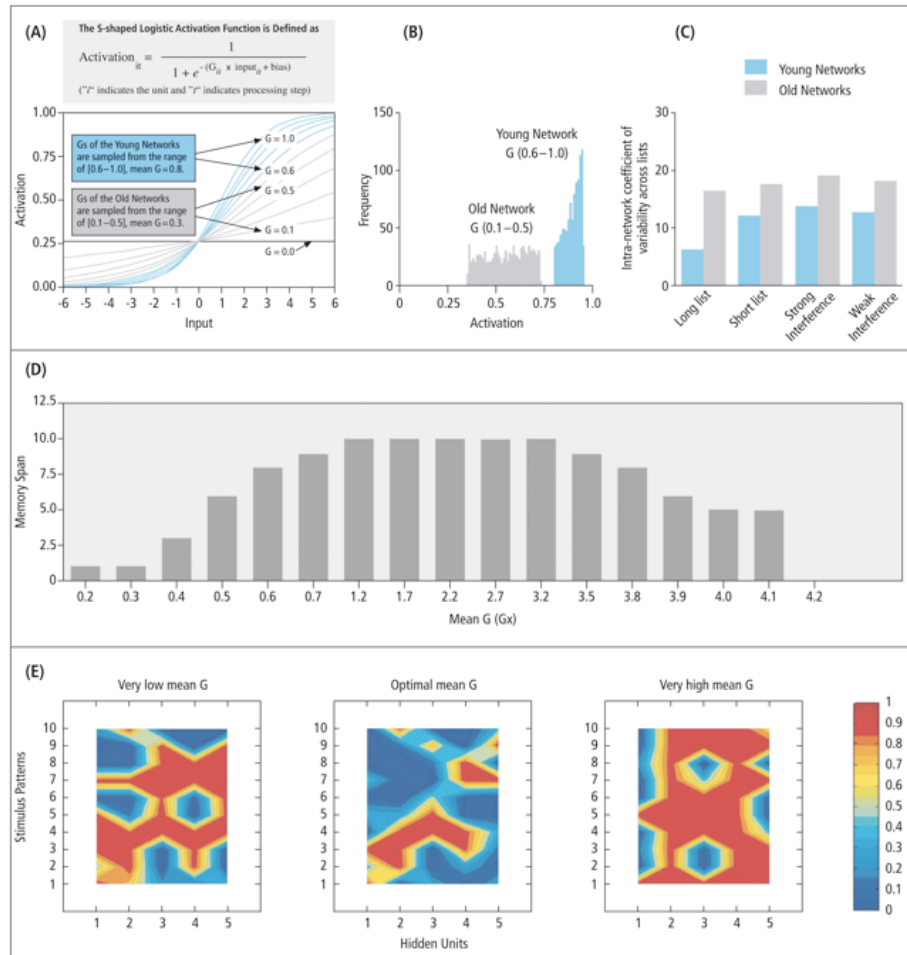
Figure 4: (A) Simulating aging-related DA modulation by reducing stochastic gain tuning. Reduced gain tuning increases (B) random activation variability and (C) performance variability in simulated old networks. (adapted, with permission from Li et al., Copyright Elsevier 2001). Stochastic gain tuning captures the inverted-U function relating DA modulation and functional outcomes of (D) memory performance and (E) distinctiveness of activation patterns (adapted, with permission from Li & Sikström, Copyright Elsevier 2002).

of neuronal representation, and cognitive outcomes such as working memory capacity. This inverted-U relation has been confirmed empirically in animal studies (e.g., Arnsten 1998; Goldman-Rakic et al. 2002) and human studies investigating the interactions of COMT gene polymorphism and pharmacology in affecting cognitive deficits observed in schizophrenics (Mattay et al. 2003). In summary, both deficient and excessive dopaminergic modulation hamper neural

information processing, and result in less distinctive neuronal representations and compromised functional behavioral outcomes.

4. Outlook: Impacts of Deficient Neuromodulation on Decision Making in Old Age

Thus far, there are two strands of empirical and computational evidence supporting *(i)* the pertinent roles of dopamine in reward-based decision making and *(ii)* pervasive declines in the efficacy of dopaminergic modulation during aging. However, the triadic relation between aging, neuromodulation, and decision making has not been directly examined. Only recently had two studies investigated neurofunctional correlates of reward-based decision making in the context of aging. Using a probabilistic object reversal task, Mell et al. (2005) found deficits in instrumental learning in older adults. Compared to younger adults, older adults showed poorer performance, i.e. they collected less reward points throughout the task and needed more trials to learn the stimulus response associations. In subsequent analyses, the poor behavioral performance in older adults was found to be associated with reduced ventral striatal brain activation in older adults (Mell et al. 2007). Related to this, another recent study found that younger and older adults differed in both self-reported and neural responsiveness to anticipated monetary gains and losses (Larkin et al. 2007). Specifically, this evidence indicates intact striatal and insular activation in older adults during gain anticipation, but a reduction in activation during loss anticipation. Both studies, however, did not directly examine the impact of aging-related decline in dopaminergic modulation in affecting the neurofunctional correlates of reward-based decision making.

The approach of stochastically reducing the slope of the sigmoidal activation for simulating aging-related declines in dopaminergic modulations can be extended to model and generate predictions for the effects of aging neuromodulation on reward-based decision making. Specifically, in the framework of temporal difference models of reward prediction, the slope of the sigmoidal function relating dopamine-modulated reward prediction and its impact on choice probability can be stochastically attenuated to simulate the effects of aging. Deriving from the computational principles observed in modeling aging neuromodulation, it can be expected that both the reward prediction signal and the mapping between reward predictions and choice actions could be noisier in older adults due to deficient dopaminergic modulation. The noisier processing at each step of the reward learning history could accumulate and might results in less distinctive representation of reward values between options, consequently affecting goal-directed reward selection. These general principles can be applied to account for aging differences in specific aspects of decision making, for instance, risk perception and preference.

As reviewed above, economic theories take the variance associated with a given expected value of a choice as an objective indicator of risk. If the aging brain shows greater variability in reward prediction (due to deficits in neuromod-

ulation) independent of the actual variance in the environment (e.g., objective variance in the expected return of investment portfolios), then older adults may have a harder time in evaluating the relative risk between different choice options. Consequently, they may not be sensitive enough to the outcomes of suboptimal choices in order to make adaptive adjustments both at the neurofunctional and behavioral levels. Furthermore, the inverted-U function relating dopaminergic modulation and functional outcomes also suggests that even in younger adults, if their dopamine level is raised beyond optimal as in the case of drug addiction or in conditions with exceedingly high reward accounts that trigger excessive phasic dopamine modulation (admittedly this would be a provocative prediction), then younger adults may also be less sensitive to risk or loss.

Interestingly, a combined experimental and computational modeling study on instrumental learning in the Iowa Gambling task indeed showed less consistency between choice behavior and outcome expectancy (i.e., noiser choice behavior) in samples of individuals with Asperger's syndrome or damages in the ventromedial prefrontal cortices or in the insular cortex. The study also included a healthy old adult sample. Older adults' choice behavior in this task, however, was found to be more consistent than that of the younger adults (Yechiam et al. 2005). It needs to be underscored that the estimated greater consistency in older adults was at the same time coupled with an estimate of greater attention to reward gain as well. It remains to be investigated whether older adults always show greater attention to gain, and how choice consistency may differ if gain expectancy is changed across decision contexts or differed between individuals.

Taken together, the theoretical predictions relating aging, neuromodulation, and reward-based decision making await rigorous empirical testing. Combing extant computational theories of dopamine modulation of reward-based decision making with models of aging-related decline in dopaminergic modulation may help generate and focus research questions on the quality of reward representation as well as the binding between reward prediction and adaptive choice for future studies on aging and neuroeconomics.

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