“Modeling Decision Making under Risk using Neurochemistry”, working paper (2010) by Chew, Ebstein, Zhong

*Abstract***.** Challenges to the descriptive validity of the expected utility model have led to the development of non-expected utility models of decision making under risk including prospect theory which incorporates psychological considerations to account for the loss-gain differentiation in risk attitude and overweighting of small probabilities associated with sizable outcomes. We propose a neurochemical extension of prospect theory by linking two evolutionarily ancient neurotransmitters – dopamine and serotonin – to the valuation and saliency of outcomes over gains and losses. This model provides a biological basis for the phenomenon of loss aversion, diminishing valuation sensitivity towards gains and losses, and nonlinear response to probabilistic stimuli. We derive its testable implications linking the decision maker’s genetic makeup modulating her dopamine and serotonin tones to her attitude towards the fourfold risks of moderate prospects, moderate hazards, longshot prospects, and longshot hazards. The empirical validity of our model is corroborated by evidence from within-subject correlations of attitude towards fourfold risks as well as evidence from recent published findings on the molecular genetics of risk taking.

“Sex-Hormone Genes Predict Gender Difference in Ultimatum Game Responder Behavior, working paper (2010) by Chew, Ebstein, Zhong”

Abstract. Despite a substantial literature on gender difference in preference, few findings have been conclusive. Combining the methodologies of experiment economics and molecular genetics, we find ultimatum game responder behavior observed in an incentivized choice setting is associated with well-characterized repeat polymorphisms of sex-hormone receptor genes. Specifically, androgen receptor gene is significantly associated with ultimatum game responder behavior of male but not female while estrogen receptor β gene is significantly associated with ultimatum game responder behavior of female but not male. Our finding seems to demonstrate conclusively a gender difference in fairness preference at the level of sex-hormone genes.

“Imaging Genomics supports Dual System for Utility of Risks over Gains and Losses”, working paper (2010) by Zhong, Chark, Ebstein, Chew

Abstract. One tenet of behavioral economics is the asymmetry in how decision makers evaluate risks involving probable gains versus risks involving likely losses. Correspondingly, an increasingly important question has been on the neuroanatomical and the neurochemical correlates of valuation over gains and losses. This paper contributes to resolving this question by combining the methodologies of brain imaging and neurogenetics. We find enhanced striatal activation responding to increases in the magnitude of utility for risks over gains and in the magnitude of disutility for risks over losses, while increased amygdala activation correlates only with the disutility of loss oriented risks. Stratifying brain activation by genotype, we further find that the DAT1 and COMT dopaminergic polymorphisms mediate striatum responses for gain oriented risks while the SLC6A4 and MAOA serotonergic polymorphisms mediate amygdala responses for loss oriented risks. Together, they suggest the role of serotonin-amygdala system in evaluating losses, which supports the hypothesis of 5HT being been linked to DA in an “opponent partnership”.

“Genetics of Human Social Behavior”, *Neuron* (2010) by Ebstein, Israel, Chew, Zhong, Knafo

Abstract. Human beings are an incredibly social species and along with eusocial insects engage in the largest cooperative living groups in the planet's history. Twin and family studies suggest that uniquely human characteristics such as empathy, altruism, sense of equity, love, trust, music, economic behavior, and even politics are partially hardwired. The leap from twin studies to identifying specific genes engaging the social brain has occurred in the past decade, aided by deep insights accumulated about social behavior in lower mammals. Remarkably, genes such as the arginine vasopressin receptor and the oxytocin receptor contribute to social behavior in a broad range of species from voles to man. Other

polymorphic genes constituting the usual suspectsi.e., those encoding for dopamine reward pathways, serotonergic emotional regulation, or sex hormonesfurther enable elaborate social behaviors.

"Dopamine D4 Receptor Gene Associated with Fairness Preference in Ultimatum Game", *PLoS ONE* (2010) by Zhong, Israel, Shalev, Xue, Ebstein, Chew

Abstract. In experimental economics, the preference for reciprocal fairness has been observed in the controlled and incentivized laboratory setting of the ultimatum game, in which two individuals decide on how to divide a sum of money, with one proposing the share while the second deciding whether to accept. Should the proposal be accepted, the amount is divided accordingly. Otherwise, both would receive no money. A recent twin study has shown that fairness preference inferred from responder behavior is heritable, yet its neurogenetic basis remains unknown. The D4 receptor (DRD4) exon3 is a well-characterized functional polymorphism, which is known to be associated with attention deficit hyperactivity disorder and personality traits including novelty seeking and self-report altruism. Applying a neurogenetic approach, we find that DRD4 is significantly associated with fairness preference. Additionally, the interaction among this gene, season of birth, and gender is highly significant. This is the first result to link preference for reciprocal fairness to a specific gene and suggests that gene × environment interactions contribute to economic decision making.

"A neurochemical approach to valuation sensitivity over gains and losses", *Proceedings of the Royal Society B* (2009) by Zhong, Israel, Xue, Sham, Ebstein, Chew

Abstract. Prospect theory proposes the hypothesis that people have diminishing sensitivity in valuing increases in the size of monetary outcomes, for both gains and losses. For decision-making under risk, this implies a tendency to be risk-tolerant over losses while being generally risk averse over gains. We offer a neurochemistry-based model of the diminishing valuation sensitivity hypothesis. Specifically, we propose that dopamine tone modulates the sensitivity towards valuation of gains while serotonin tone modulates the sensitivity towards valuation of losses. Consequently, higher dopamine tone would yield a more concave valuation function over gains while higher serotonin tone would yield a more convex valuation function over losses. Using a neurogenetics strategy to test our neurochemical model, we find that subjects with the 9-repeat allele of DAT1 (lower DA tone) are more risk-tolerant over gains than subjects with the 10-repeat allele, and that subjects with the 10-repeat allele of STin2 (higher 5HT tone) are more risk-tolerant over losses than subjects with the 12-repeat allele. Overall, our results support the implications of our model and provide the first neurogenetics evidence that risk attitudes are partially hard-wired in differentiating between gain- and loss-oriented risks.

"Monoamine Oxidase A Gene (MAOA) Associated with Attitude Towards Longshot Risks", *PLoS ONE* (2009) by Zhong, Israel, Xue, Sham, Ebstein, Chew

Abstract. Decision making often entails longshot risks involving a small chance of receiving a substantial outcome. People tend to be risk preferring (averse) when facing longshot risks involving significant gains (losses). This differentiation towards longshot risks underpins the markets for lottery as well as for insurance. Both lottery and insurance have emerged since ancient times and continue to play a useful role in the modern economy. In this study, we observe subjects' incentivized choices in a controlled laboratory setting, and investigate their association with a widely studied, promoter-region repeat functional polymorphism in monoamine oxidase A gene (MAOA). We find that subjects with the high activity (4-repeat) allele are characterized by a preference for the longshot lottery and also less insurance purchasing than subjects with the low activity (3-repeat) allele. This is the first result to link attitude towards longshot risks to a specific gene. It complements recent findings on the neurobiological basis of economic risk taking.

“The Heritability of Attitude Toward Economic Risk”, *Twin Research and Human Genetics* (2009) by Zhong, Set, Zhang, Xue, Sham, Ebstein, Israel, Chew

Abstract. The propensity to take risk underpins a wide variety of decision-making behavior, ranging from common ones such as asking for directions and trying out a new restaurant to more substantial economic decisions involving, for instance, one's investment or career. Despite the fundamental role of risk attitude in the economy, its genetic basis remains unknown. Using an experimental economics protocol combined with a classical twin strategy, we provide the first direct evidence of the heritability of economic risk attitude, at 57%. We do not find a significant role for shared environmental effects, a common observation in behavioral genetics that is contrary to commonly held views in economics. Our findings complement recent neuroeconomic studies in enhancing the understanding of the neurobiological basis of risk taking.