New approaches to investigating social gestures in autism spectrum disorder

Kenneth T Kishida[1], Jian Li[2], Justin Schwind[3] and Pendleton Read Montague[1,4,5,6*]

The combination of economic games and human neuroimaging presents the possibility of using economic probes to identify biomarkers for quantitative features of healthy and diseased cognition. These probes span a range of important cognitive functions, but one new use is in the domain of reciprocating social exchange with other humans - a capacity perturbed in a number of psychopathologies. We summarize the use of a reciprocating exchange game to elicit neural and behavioral signatures for subjects diagnosed with autism spectrum disorder (ASD). Furthermore, we outline early efforts to capture features of social exchange in computational models and use these to identify quantitative behavioral differences between subjects with ASD and matched controls. Lastly, we summarize a number of subsequent studies inspired by the modeling results, which suggest new neural and behavioral signatures that could be used to characterize subtle deficits in information processing during interactions with other humans.

Keywords: Autism spectrum disorder, Social exchange, Reciprocation, Game theory, Computational models, Functional magnetic resonance imaging, Biomarker

The challenges of social exchange are shared throughout the animal kingdom [1-3]. Humans engage in repeated reciprocal interactions with kin and non-kin; this has required our species to develop a particular capacity to track these interactions and assign credit and blame accordingly [3-6]. The underlying neurobiological mechanisms underlying these abilities in humans remain an open area of investigation, which is generating insight into a number of mental illnesses including autism spectrum disorders (ASD) [7-18].

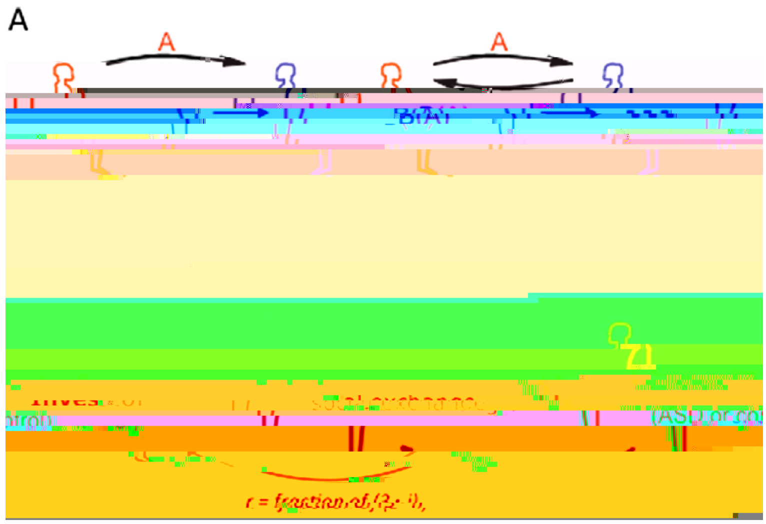
One important challenge for an agent engaged in social exchange is the ability to generate models of others' mental states, a capacity referred to as 'theory of mind' [19,20]. Human neuroimaging experiments have implicated a consistent set of brain regions hypothesized to be involved in this process [21-24]. The role of this kind of computation and others are exemplified in even the simplest exchanges. For instance, in a fair trade the brains of the interacting agents must be able to: (1) compute norms for what is considered fair; (2) detect deviations from such norms; and (3) select appropriate actions based on these deviations.

Reciprocating social exchanges and their related computations occur in our daily lives and are the basis for a number of staged interactions in clinical practice. However, the computations themselves likely occur well below our threshold for conscious experience. For example, in the diagnostic procedures for ASD a trained professional interacts with a suspected patient and navigates a predetermined series of give-and-take scenarios (for example, the Autism Diagnostic Observation Scale (ADOS) [25]); during this interaction the clinician tries to detect typical and atypical social gestures based on trained-up (for example, experience-based) expectations of behavior. Additionally, insight into the patient's social cognitive process is sought using interviews of the patient and family members [26,27].

Computational approaches in combination with quantitative probes of behavior (for example, game theoretic paradigms [28,29]) promise to reveal underlying dimensions of healthy human decision-making and thereby will provide a basis for which to compare against

* Correspondence: read@vt.edu
[1]Human Neuroimaging Laboratory and Computational Psychiatry Unit, Virginia Tech Carilion Research Institute, Roanoke, VA 24016, USA
[4]Department of Physics, Virginia Tech, Blacksburg, VA 24061, USA
Full list of author information is available at the end of the article

in psychiatric populations [30,31]. These approaches promise to excel, over traditional approaches, in capturing quantitative normative behavior and associated neurobiological responses. In these tasks participants are required to make decisions under incentivized conditions; the incentive is typically a monetary one and the decision spaces are restricted by the particular game [28]. The games may be against a ‘roll of the dice’ or against real or simulated agents (for example, other humans or computer simulations) and can be employed though a computer interface. These conditions can augment traditional diagnostic procedures by providing additional behavioral and neurobiological measurements. In computer-based game play, the behaviors elicited and signals exchanged between players are all captured within the patient-computer interface. These measurements can then be directly ported into tests over competing computational models about hypothesized cognitive processes underlying social behavior. In addition, variables within the games are designed to be parametric, which provides increased specificity in the analysis of associated brain responses. The use of the internet and technologies like hyperscanning, which synchronizes fMRI scanners and study participants over the internet [32], has already and will continue to allow more complex social exchange to be studied while allowing experimenters to have control over which signals are exchanged. These methods take highly complex social interactions and reduce the exchanges to simpler, more tractable, dimensions for quantitative analysis; and, have recently been applied to the neurobiological investigation of social exchange [33-38]. Fairness and cooperation games dominate these recent efforts because they assess a subject’



Two-party social exchange games to probe autism spectrum disorder neurobehavioral responses. (**A**) Two-party repeated interaction games with feedback and learning. Two-party signaling games allow for the investigation of social exchange between two (or more) agents. The signals sent between participants are controlled such that the information sent and the information that must be inferred is explicit and controlled by the experimenter. Multi-round games allow for the development of reputation and the opportunity for learning and adapting, which allow for the study of interesting social dynamics in a controlled and objectively quantitative manner. (**B**) Multi-round trust game. The multi-round trust game is a 10-round repeated interaction between the same two partners. Player 1 ('investor') is endowed with 20 points and is to decide how much, if any, to share with the 'trustee' (player 2); the amount shared is tripled on its way to the trustee; the trustee then decides how much, if any, to repay to the investor; at the end of each round the total points earned/kept by each player is put into a 'bank'; and the subsequent round begins with a new endowment of 20 points.

points and the totals at the end of each round are put aside to be tallied up at the very end of the game; (8) at the end of 10 rounds the totals in the bank for each player determines how much real money they will be paid and is how the game is incentivized: the more points one earns the more real money they will take home. To earn the most points possible the players must cooperate; however, generous signals of cooperation can be taken advantage of and a player may cheat the other out of an equal distribution of the profits.

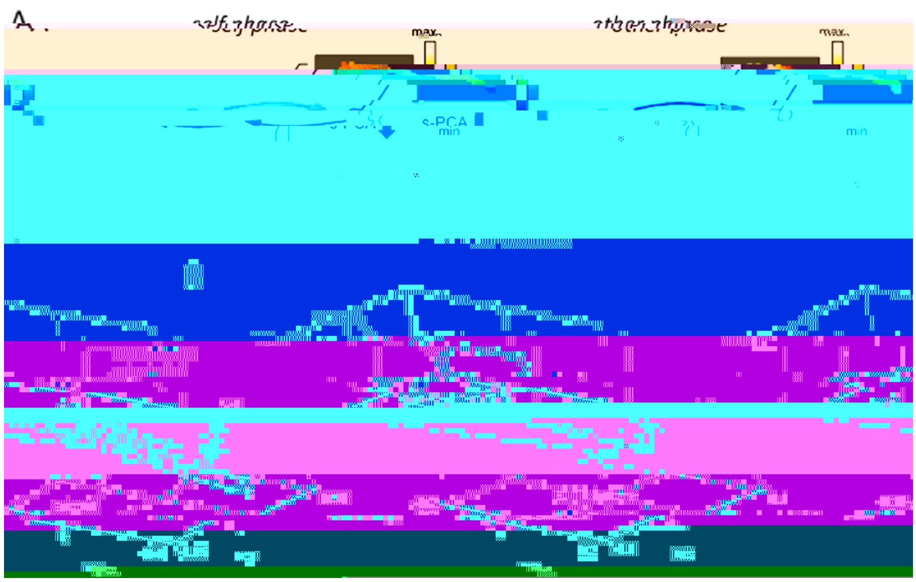
The stag-hunt game also engages two participants and also requires participants to cooperate to achieve maximal gains. The goal of the game is to 'hunt' either a 'stag' (big profits) or a 'rabbit' (smaller profits). The players see a game board where they can move one square at a time and do so sequentially. In this manner, the participants observe the behavior of their partner and attempt to infer whether the move was intended to hunt the stag (cooperate) or a rabbit (defect). The rabbits do not move and are positioned on the board such that they can be hunted by the efforts of a single player, but provide a small payoff; on the other hand, two players must cooperate to hunt the stag and are rewarded for doing so with a bigger point value. Each move in the game that does not collect either a rabbit or a stag is viewed as a cost and diminishes a player's point total. In the implementation of this game by Yoshida and colleagues the stag moved first, then the human participant, then a computer agent partner [45]. Like the multi-round trust game the players point totals are directly tied to the amount of real money they will take home at the end of the experiment, thus incentivizing participants to make truthful expressions of their preferences and assessments of the game state.

Yoshida and colleagues' results from applying the stag-hunt game to investigate hidden cognitive processes such as belief inference in autistic populations is particularly promising for our understanding of ASD and for computational and game theoretic approaches to investigating the heterogeneity known to exist within the spectrum [45]. The application of their 'game theory of mind' [43] demonstrated an ability to differentiate ASD symptom severity by a parameter in their model related to the patient's ability to infer the strategic sophistication of their partner; the authors clarify this as the ability to infer the partner's mindreading strategy. Additionally this parameter was distinct from the models estimate of patients' ability to plan iteratively, which was not related to symptom severity, but rather showed a strong correlation with intellectual ability as assessed by verbal and non-verbal intelligence tests [45].

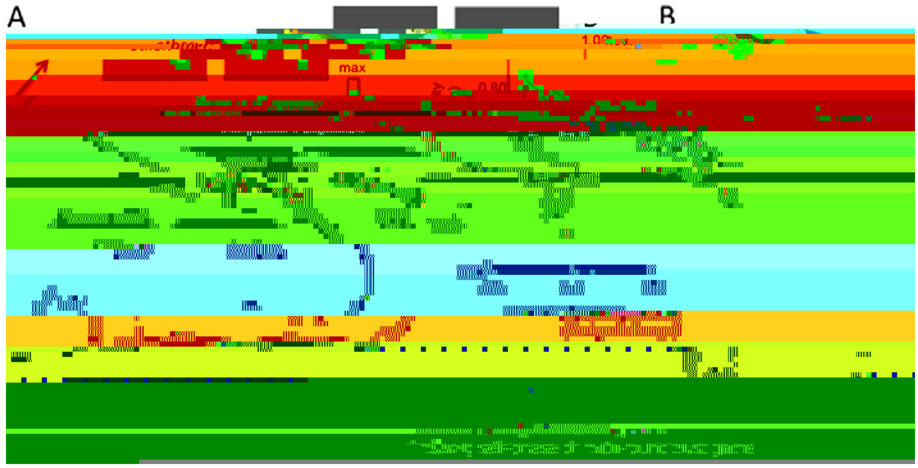
Early results from the multi-round trust game

The multi-round trust game has been used to investigate social exchange in pairs of healthy individuals [34,46-48] and pairs consisting of a healthy investor and a trustee diagnosed with a psychiatric disorder including: ASD [46,48], borderline personality disorder [48,49], major depression [48], and attention deficit hyperactivity disorder [48]. Tomlin and colleagues identified a specific response pattern along the anterior to posterior axis of the cingulate cortex [47]. They identified that a spatial pattern of activity that corresponded with ‘self’ and ‘other’ phases of the trust game exchange. This agent-specific response did not modulate with the number of points exchanged, the character of the gesture (benevolent or malevolent [34,47]), or role (investor or trustee) of the player; the response pattern was specific to who was acting at that particular stage of the game (that is, ‘me’ or ‘not me’). Additionally, the agent-specific pattern of activity was absent when the players participated in a control experiment where the partner was absent and the players knowingly engaged in a computer-driven task [47]. This result suggested that the cingulate ‘self’ and ‘other’ response patterns may be affected in special populations where these signals would be important for social exchange.

Chiu and colleagues tested this hypothesis by investigating social pairs consisting of a healthy investor and a trustee diagnosed with ASD [46]. This work shed light on the role of the agent-specific cingulate response patterns during social exchange and on altered neural responses in patients diagnosed with ASD. The authors used an analytical approach to disentangle various modes of operation in the cingulate cortex using principal components analysis applied to spatio-temporal data measured in the cingulate during the social exchange game. One mode they identified matched the previously observed agent-specific response profile and was named the ‘self-eigenmode’ due to the specific phase of social exchange in which it was elicited (Figure 2). Determining the self-eigenmode allows the reduction of the spatial pattern of activity to a single dimension and compares the role this ‘response pattern’ plays in social exchange iterations. Chiu and colleagues went on to show that this pattern was also elicited during perspective taking shifts in a structured imagery task [46] and demonstrated that participants with ASD showed diminished responses along the self-eigenmode specifically during the self-phase of the trust game (Figure 3A [46]). These results led to the demonstration that a region in the middle cingulate cortex (the peak regions in the self-eigenmode)



Spatial principal components analysis identifies ‘self-eigenmode’ response during social exchange (adapted from [46]).
(**A**) Cingulate hemodynamic responses from the trustees’ brain during the ‘self’ and ‘other’ phases of the multi-round trust game. The spatially defined domains along the posterior to anterior axis were subjected to principal components analysis. Among the principal components identified was the ‘self-eigenmode’, which captures the dynamic agent-specific spatio-temporal activity in the cingulate as the trust game evolves. The self-eigenmode flips its sign as the game transitions from the self-phase to the other phase of the trust game. (**B**) Phase dynamics of other’ phases esD(r)-31rsf-32.0259-1.16.125



ASD trustees show diminished cingulate self-response pattern during social exchange in the multi-round trust game (adapted from [46]). (**A**) Diminished cingulate response pattern during 'self–phase' of the iterated multi-round trust game. The ' showed diminished activity in the ASD participants that correlated with their symptom scores on the Autism

is bounded; in other words, that it does not not go on

36. Rilling JK, Sanfey AG, Aronson JA, Nystrom LE, Cohen JD: The neural correlates of theory of mind within interpersonal interactions. 2004, 22:1694–1703.
37. Sanfey AG, Rilling JK, Aronson JA, Nystrom LE, Cohen JD: The neural basis of economic decision-making in the ultimatum game. 2003, 300:1755–1758.
38. Singer T, Seymour B, Apos O, Doherty J, Stephan K: Empathic neural responses are modulated by the perceived fairness of others. 2006, 439:466–469.
39. Berg J, Dickhaut J, McCabe K: Trust, reciprocity, and social history. 1995, 10:122–142.
40. Camerer CF, Fehr E: When does "economic man" dominate social behavior? 2006, 311:47.
41. Kagel JH, Roth AE: . Princeton, NJ: Princeton University Press; 1995.
42. Montague PR, Lohrenz T: To detect and correct: Norm violations and their enforcement. 2007, 56:14–18.
43. Yoshida W, Dolan RJ, Friston KJ: Game theory of mind. 2008, 4:e1000254.
44. Yoshida W, Seymour B, Friston KJ, Dolan RJ: Neural mechanisms of belief inference during cooperative games. 2010, 30:10744.
45. Yoshida W, Dziobek I, Kliemann D, Heekeren HR, Friston KJ, Dolan RJ: Cooperation and heterogeneity of the autistic mind. 2010, 30:8815.
46. Chiu PH, Kayali MA, Kishida KT, Tomlin D, Klinger LG, Montague PR: Self responses along cingulate cortex reveal quantitative neural phenotype for high-functioning autism. 2008, 57:463–473.
47. Tomlin D, Kayali MA, King-Casas B, Anen C, Camerer CF, Quartz SR, Montague PR: Agent-specific responses in the cingulate cortex during economic exchanges. 2006, 312:1047–1050.
48. Koshelev M, Lohrenz T, Vannucci M, Montague PR: Biosensor approach to psychopathology classification. 2010, 6:e1000966.
49. King-Casas B, Sharp C, Lomax-Bream L, Lohrenz T, Fonagy P, Montague PR: The rupture and repair of cooperation in borderline personality disorder. 2008, 321:806.
50. Ray D, King-Casas B, Montague PR, Dayan P: Bayesian model of behaviour in economic games. 2008, 21:1345–1353.
51. Fehr E, Schmidt KM: A theory of fairness, competition, and cooperation. 1999, 114:817.
52. American Psychiatric Association: . 4th edition. Washington, DC: American Psychiatric Association; 2000.
53. Hampton AN, Bossaerts P, O'Doherty JP: Neural correlates of mentalizing-related computations during strategic interactions in humans. 2008, 105:6741.
54. Behrens TEJ, Hunt LT, Rushworth MFS: The computation of social behavior. 2009, 324:1160.
55. Nimchinsky EA, Gilissen E, Allman JM, Perl DP, Erwin JM, Hof PR: A neuronal morphologic type unique to humans and great apes. 1999, 96:5268–5273.
56. Allman JM, Hakeem A, Erwin JM, Nimchinsky E, Hof P: The anterior cingulate cortex. The evolution of an interface between emotion and cognition. 2001, 935:107–117.
57. Vogt BA, Berger GR, Derbyshire SW: Structural and functional dichotomy of human midcingulate cortex. 2003, 18:3134–3144.
58. Critchley HD: Neural mechanisms of autonomic, affective, and cognitive integration. 2005, 493:154–166.
59. Brazdil M, Kuba R, Rektor I: Rostral cingulate motor area and paroxysmal alien hand syndrome. 2006, 77:992–993.
60. Ehrsson HH, Wiech K, Weiskopf N, Dolan RJ, Passingham RE: Threatening a rubber hand that you feel is yours elicits a cortical anxiety response. 2007, 104:9828–9833.
61. Nemeth G, Hegedus K, Molnar L: Akinetic mutism associated with bicingular lesions: Clinicopathological and functional anatomical correlates. 1988, 237:218–222.
62. Cohen RA, Kaplan RF, Zuffante P, Moser DJ, Jenkins MA, Salloway S, Wilkinson H: Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy. 1999, 11:444–453.
63. Wallace B, Cesarini D, Lichtenstein P, Johannesson M: Heritability of ultimatum game responder behavior. 2007, 104:15631–15634.
64. Cesarini D, Dawes CT, Fowler JH, Johannesson M, Lichtenstein P, Wallace B: Heritability of cooperative behavior in the trust game. 2008, 105:3721–3726.

doi:10.1186/1866-1955-4-14
Cite this article as: Kishida: New approaches to investigating social gestures g.3(atism)300-304(f)T.atl0Fshi03729TD0Tc[7a2tio8ty)301.8.8(nTDv3481Tf8.2bAevelop