REVIEW **Open Access**

New approaches to investigating social gestures in autism spectrum disorder

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Abstract

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

Review

Games to study autism spectrum disorders

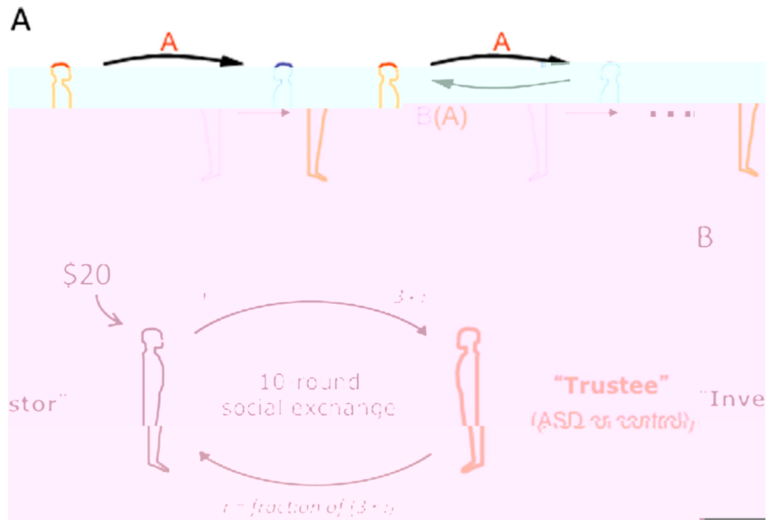

Figure 1 Two-party social exchange games to probe autism spectrum disorder neurobehavioral responses. (**A**) Two-party repeated interaction games with feedback and learning. Two-party signaling games allow for the investigation of social exchange between two (or more) agents. The signals sent between 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.

Early results from the multi-round trust game

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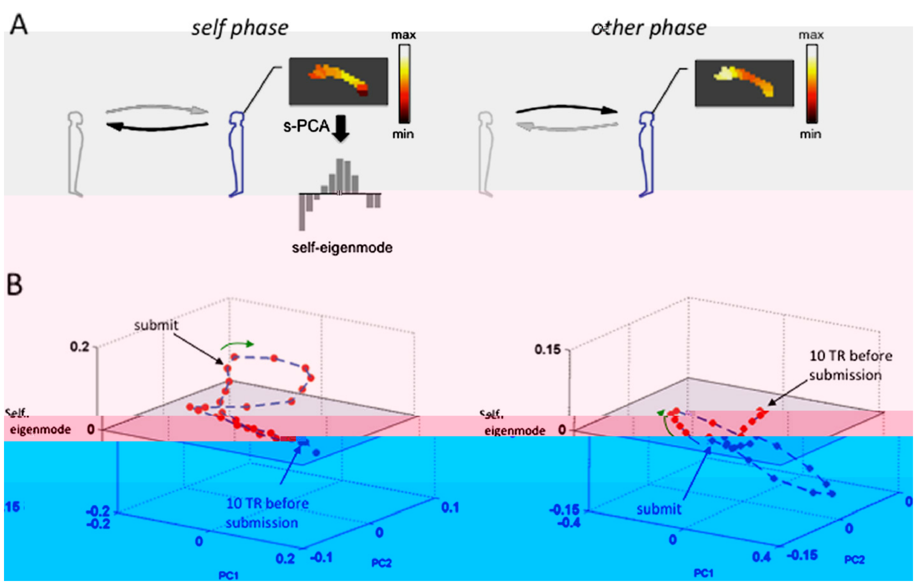

Figure 2 Spatial principal components analysis identifies 'self-eigenmode' response during social exchange (adapted from [46]). (**A**) Cingulate hemodynamic responses from the trustees' brain during the 'self' and 'other' phases of the multi-round trust game. The spatially defined domains along the 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 cingulate response during multi-round trust game. The self-eigenmode response does not evolve in isolation. Three eigenvectors characterize the full set of the cingulate self-basis. Each of the red circles is a single TR in the measurement of the BOLD response during the self and other phases of the trust game in the trustee brain. These responses are plotted in the three dimensions that comprise the cingulate self-basis and shows how the cingulate response is dynamic, yet regular and throughout repeated trials of the self and other phases of the trust game. Increased self-responses are indicated by more positive values on the self-eigenmode axis (vertical axes); whereas non-self or 'other' responses are indicated by more negative values on the self-eigenmode. On the left we observe positive values on the self-eigenmode dimension leading up to an following the submission of a repayment by the trustee; and, on the right we observe negative self-eigenmode values in the trustee brain following the submission of an investment by the investor.

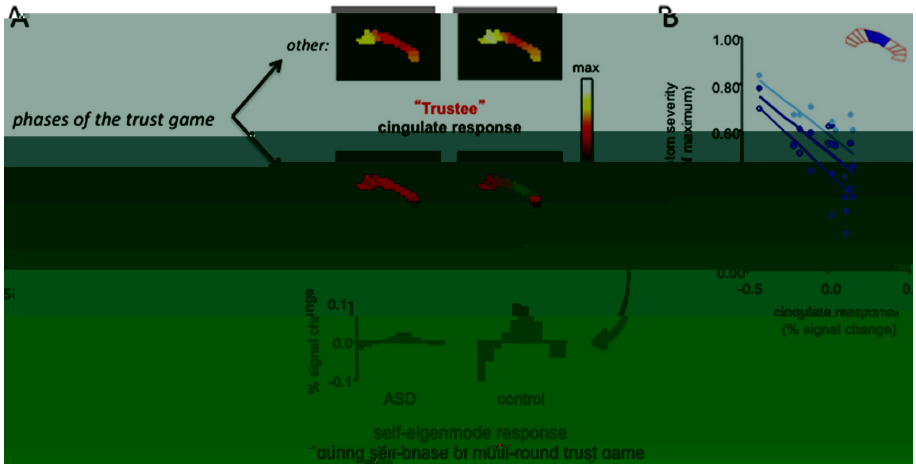

Figure 3 ASD trustees show diminished cingulate self-response pattern during social exchange in the multi-round trust game (adapted from [46]). (**A**) Diminished cingulate response pattern during 'self–phase' of the iterated multi-round trust game. The 'other' response pattern was similar in ASD (*n* = 12) and age- and IQ-matched control participants (*n* = 18). However the cingulate 'self' response was diminished in the ASD cohort. Projection of the BOLD response pattern onto the cingulate self-eigenmode reveals the contribution of that mode of operation in the cingulate, and show that it is significantly diminished in the ASD cingulate cortex. (**B**) Regions in the middle cingulate cortex show diminished response, which correlates with ASD symptom severity. The middle regions of the cingulate cortex show significant correlation with symptom severity in the ASD cohort. The less active this region is during the self-phase is correlated with the communication subscale, social subscale, and overall score on the Autism Diagnostic Interview, Revised (open circles: ADI-R communication subscale, r = −0.69, *p* = −0.012; light blue filled circles: ADI-R social subscale, r = −0.70, *p* = 0.011; dark blue filled circles: ADI-R total score, r = −0.73, *p* = 0.007).

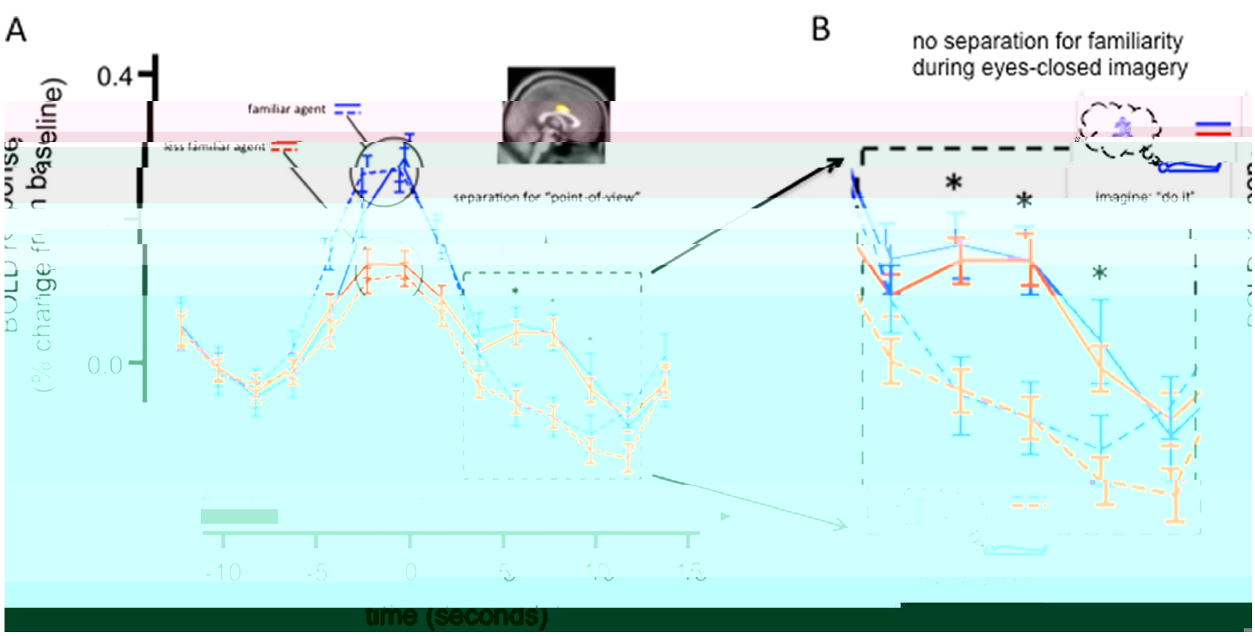

Figure 4 Middle cingulate cortex differentiates perspective taking responses during eyes-closed imagery. (**A**) Time-series of BOLD response in middle cingulate cortex during structured imagery task. (Inset: mask used in time-series analysis.) Mean BOLD response (% signal change from baseline) along the vertical axis; time (s) along the horizontal axis. Plotted: mean response of the middle cingulate cortex (MCC) ± standard error about the mean for motor-imagery trials (solid lines) and visual-imagery trials (dashed lines) for expertise-congruent conditions (blue lines) and expertise-incongruent trials (red lines). Note: the MCC responds during motor-imagery trials, but not during visual-imagery trials (solid lines *vs.* dashed lines, time-points +4 s to +12 s, see dashed box), and the MCC does not differentiate expertise-congruent trials from expertise-incongruent trials during eyes-closed visual or motor imagery (blue lines *vs.* red lines, time-points +4 s to +12 s). Asterisks: $p < 0.05$, (one-tailed t-test, *n* = 81 subjects: 'do it' > 'watch it' collapsed over congruency conditions). (**B**) Middle cingulate response during eyes-closed imagery. Familiarity with subject and action (for example, athletic expertise congruency) does not separate MCC response during eyes-closed imagery; however, first-person perspective-taking does.

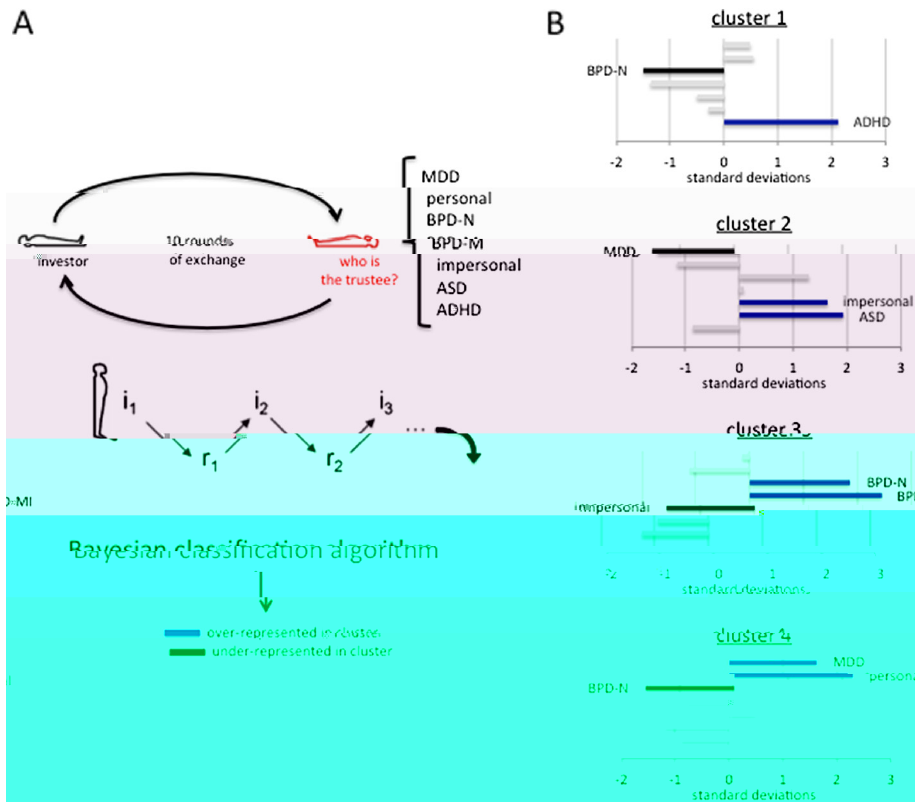

Figure 6 Classification of Trustee 'type' from Investors' behavior in two-party exchange. (**A**, **B**) Depiction of model-free clustering approach using multi-round trust game data. The data used in this approach was collected in previous studies [34,46-49] A. The multi round trust game is played between a healthy investor (black player) and a 'target' trustee (red player). The 'target' trustee was one of the following 'types': major depressive disorder (MDD), personal [47], borderline personality disorder - non-medicated (BPD-N) [49], borderline personality disorder - medicated (BPD-M) [49], impersonal [34], autism spectrum disorder (ASD) [46], and attention deficit hyperactivity disorder (ADHD) [47]. The approach described in detail in Koshelev *et al.* (2010) examines the investor behavior as a polynomial of past rounds of investments and returns (see panel B). $i_1, i_2, \ldots, i_t$ are the investments made by the investor during round t. Likewise, $r_1, r_2, \ldots, r_t$ are the repayments made by the trustee during round t. *Classification of the investor-trustee dyad*: is performed by predicting the investors' decision at round t using a polynomial where the order of the polynomial, the number of past rounds, and the number of clusters discovered are left as free parameters to be discovered. The diagnostic categories for the trustee 'type' listed in panel A are blinded in this classification procedure. Only the behavior (investments and repayments over rounds) in the multi-round trust game is used. The result of this classification determined that a first-order polynomial, two rounds back, and four clusters were optimal. (B) Resulting four clusters and classification of diagnostic categories for model-free biosensor approach. The resulting classification identified four clusters where individuals from each diagnostic category were over- (blue bars) or under-represented (black bars). Vertical axes: investor-trustee dyad types (from top to bottom): MDD, personal [47], BPD-N [49], BPD-M [49], impersonal [34], ASD [46], and ADHD [47]. Only the statistically significant categories (that is, greater than 1.5 standard deviations from the mean) are labeled in each plot. Horizontal axes: standard deviations from the mean. Figure adapted from [48].

[illegible]

[illegible]

$$U_i(x_i, x_j; \alpha_i, \beta_i) = x_i - \alpha_i max(x_j - x_i, 0) - \beta_i max(x_i - x_j, 0) \quad (1)$$

[illegible] *et al.* [50] [illegible]

$$i_t = \beta_0 + \beta_1 i_{t-1} + \beta_2 r_{t-1} + \beta_3 i_{t-2} + \beta_4 r_{t-2} \quad (2)$$

Discussion and future directions

Conclusions

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Additional files

Additional file 1: Figure S1. Structured Imagery Task.

Additional file 2: Figure S2. Structured Imagery Task elicits self and other cingulate self-eigenmode responses.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
KTK analyzed and interpreted the human imaging data regarding the perspective-taking experiments in accomplished athletes and the self and other face viewing task and is a major contributor in the writing of this manuscript. JL assisted in the analysis of the athlete data. JS assisted in collecting the athlete data. PRM designed the structured imagery task, the multi-round trust task and analysis strategies for both interpretation and writing of this manuscript. All authors have read and approved this manuscript.

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