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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

For the cases where we had previous examples of similar research we conducted power analyses using G*Power software (Faul, F., Erdfelder, E., Lang, A. G. & Buchner, A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior research methods 39, 175-191 (2007)) applied to the previous studies. In cases of novel paradigms tested here for the first time we used sample sizes optimized for power at normal distribution, typically 40 participants (20 per group) in a within-subjects repeated measures design. In all cases we estimated and reported Cohens d' as a measure of resultant power. Finally, we also conducted p_curve analysis to guard against biased reporting (Simonsohn, U., Nelson, L. D. & Simmons, J. P. P-curve and effect size: Correcting for publication bias using only significant results. Perspectives on Psychological Science 9, 666-681 (2014))

Notably, our cohort of 35 participants with ASD overall, and ~20 participants per individual experiment is relatively large in comparison to typical studies collecting autonomic physiology measures from adults with ASD.

2. Data exclusions

Describe any data exclusions.

Exclusions were according to previously published criteria.
For EDA: We applied exclusion criteria according to Green et al. This included exclusion of participants with no EDA reactivity at all, i.e., EDA under 0.02 μS, or with excessive motion. This resulted in the exclusion of 1 TD and 3 ASD participants from ER-EDA in the Faces task in Experiment 2, and 5 ASD participants from ER-EDA in the Stroop task in Experiment 2. In experiment 4, one TD participant had no EDA recording due to technical fault.
For startle: We applied exclusion criteria according to Pause, Prehn, and Blumenthal. The startle response is typically observed in a time window of 30-90 ms following the acoustic stimulus. Events in which the maximum amplitude in this temporal window was higher than the maximum amplitude within the 100 ms pre-stimulus baseline by a factor of 2.5 were considered as responses. Participants that had at least 5 responses in each condition were considered as responders. According to this criterion, 1 TD participant was excluded from further analysis. One ASD participant was excluded because his mean EMG amplitude exceeded more than 3 SD from mean EMG amplitude of all participants.

3. Replication

Describe whether the experimental findings were reliably reproduced.

For the revision we replicated two paradigms (Faces and Stroop) in 8 additional subjects with striking replicability (Figure in Reply to Referee document)

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

For subject selection, no randomization, nor preselection was used. This is because we have one group of TD and one of ASD, so we obviously cannot assign across groups. We did, however, randomize trial order within experiments, and counter-balanced conditions across subjects.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

All subjects were blind to condition in all experiments.
Experimenters were also blind to condition in experiment with AND and in the behavioral fear Experiment (the Manikin Experiment).

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

For general statistical analysis we used Statistica for Windows and Matlab. We used G*Power for power analysis, and Chart 7 for mac (AD Instruments) for analyzing autonomic measures.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

No restrictions

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

No antibodies used in the study

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

No eukaryotic cell line used in the study

b. Describe the method of cell line authentication used.

NA

c. Report whether the cell lines were tested for mycoplasma contamination.

NA

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

NA

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

NA

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

A total of 35 (2F) cognitively able adult participants with ASD (Table 1) and 81 (2F) TD matched controls participated in the reported experiments. All individuals in the ASD group were assessed by experienced clinicians independent of the present study and met DSM (mostly -IV) diagnostic criteria for an ASD. The TD and ASD cohorts did not differ in age (TD = 27.3 ± 3.3 years; ASD = 26.3 ± 6.0 years, $t(99) = 1.1$, $p = 0.29$) only slightly but significantly differed in years of education (ASD = 13.3 ± 2.6, TD = 14.8 ± 1.6, $t(96) = 3.6$, $p < 0.001$), and as intended, significantly differed in autism quotient (AQ) score (ASD = 24.7 ± 6.5, TD = 16.5 ± 4.7, $t(98) = 7.2$, $p < 0.0001$).