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Inflexible Updating of the Self-Other Divide During a Social Context in Autism: Psychophysical, Electrophysiological, and Neural Network Modeling Evidence

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ABSTRACT

BACKGROUND: Autism spectrum disorder (ASD) affects many aspects of life, from social interactions to (multi) sensory processing. Similarly, the condition expresses at a variety of levels of description, from genetics to neural circuits and interpersonal behavior. We attempt to bridge between domains and levels of description by detailing the behavioral, electrophysiological, and putative neural network basis of peripersonal space (PPS) updating in ASD during a social context, given that the encoding of this space relies on appropriate multisensory integration, is malleable by social context, and is thought to delineate the boundary between the self and others.

METHODS: Fifty (20 male/30 female) young adults, either diagnosed with ASD or age- and sex-matched individuals, took part in a visuotactile reaction time task indexing PPS, while high-density electroencephalography was continuously recorded. Neural network modeling was performed in silico.

RESULTS: Multisensory psychophysics demonstrates that while PPS in neurotypical individuals shrinks in the presence of others—as to "give space"—this does not occur in ASD. Likewise, electroencephalography recordings suggest that multisensory integration is altered by social context in neurotypical individuals but not in individuals with ASD. Finally, a biologically plausible neural network model shows, as a proof of principle, that PPS updating may be inflexible in ASD owing to the altered excitatory/inhibitory balance that characterizes neural circuits in animal models of ASD.

CONCLUSIONS: Findings are conceptually in line with recent statistical inference accounts, suggesting diminished flexibility in ASD, and further these observations by suggesting within an example relevant for social cognition that such inflexibility may be due to excitatory/inhibitory imbalances.

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Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by altered social interactions, repetitive and restricted behaviors, and differences in language and communication skills. The current diagnosis rate of ASD is approximately 1 in 59 children in the United States (1), and in addition to growing in pervasiveness, it is a condition growing in scope. Beyond the established core features in the social domain, sensory processing differences are increasingly recognized in ASD (2). In fact, atypical sensory responses are now part of the ASD diagnostic criteria (DSM-5).

Two overarching themes have emerged in the study of sensory function in ASD. The first of these comes from animal model work and highlights a marked hypersensitivity of neurons during weak sensory stimulation in mouse models of autism (3,4). In principle, these changes could be a property of the neurons themselves, but they are more widely considered to be a circuit property (5) reflecting changes in the balance of excitation and inhibition (6,7). The second, derived largely from the human literature, suggests that while individuals with ASD may outperform their neurotypical counterparts in local sensory processing (8), they present with decreased holistic processing (9). A similar conclusion applies to the ability to integrate information across different sensory modalities, with a growing body of evidence pointing to atypical multisensory integration in ASD (10,11)—but see (12) for opposing evidence.

Now, bridging across the core social deficits that characterize ASD (clinical observations), their phenotypic-level sensory processing (dis)abilities (e.g., multisensory integration [human studies]), and their putative underlying neural implementation (e.g., excitatory/inhibitory [E/I] imbalance [animal studies]) is a notorious challenge. Arguably, this endeavor requires both 1) the appropriate computational tools to bridge across levels of description (i.e., from neurons to behavior) and 2) an experimental paradigm that is germane to both social and sensory processing.

In this study, we attempt to start bridging this gap by 1) studying the boundary between the self and others in autism and its updating to different social contexts, 2) deriving the electroencephalographical (EEG) correlates of social updating of the space where multisensory integration is likely to occur (for visuotactile pairings, this is the space near the body), and 3) proposing via a biologically plausible neural network model a proof-of-principle account of the underlying neural circuitry that may be distinct in individuals with ASD versus neurotypical control subjects. The neural network modeling is a proof of principle, as we simply detail one of potentially many different mechanisms that could have engendered the observed differences between individuals with ASD and control subjects. More precisely, individuals with ASD are known to be “personal space invaders” (13,14). In natural settings, they routinely bump into others, or will come stand too near you during conversation, being unaware of social norms regulating the space between individuals. Conveniently, this social function may be closely related to the encoding of peripersonal space (PPS) (15)—the space immediately adjacent to and surrounding the body—and we understand this encoding well. PPS coding is subserved by multisensory neurons with tactile receptive fields (RFs) on the body (or body parts) and visual RFs in a depth-limited zone near the body. Furthermore, PPS is thought to implicitly delineate the space of the self versus that of other agents (16–18), and both physiological recordings in monkeys (19) and psychophysical tasks in healthy humans have suggested that the PPS is malleable to social context, reshaping as a function of the quality of social interaction (20) or even perceived morality of others (21). Finally, biologically plausible neural network models of PPS have been proposed (22–24), and these models are able to recapitulate the basic properties of PPS encoding. In turn, PPS encoding subserves aspects of social life and is reliant on appropriate (multi)sensory processing, and we have computational tools attempting to bridge from behavior to putative neurons. Altogether, by studying remapping (or resizing, used interchangeably throughout the text) of PPS in ASD during a social context, we can bridge from social function (i.e., self vs. other, impact of social setting) to sensory processing (i.e., multisensory integration in the near space), while rooted in a precise and biologically plausible (albeit admittedly underconstrained) neural network model.

METHODS AND MATERIALS

Briefly, to measure PPS, we asked participants to respond as fast as possible to touch on their hand as visual stimuli were presented at different distances (Figure 1A) and EEG was recorded. Half of the blocks of trials were nonsocial, and half were social, where an experimenter sat facing the participant at a distance of 150 cm with a neutral expression (Figure 1A). See the Supplement for details.

RESULTS

Smaller PPS During Social Context in Neurotypical but Not Individuals With ASD

Overall, participants showed a very low omission rate (2.9%, contrast between ASD and control subjects, $p = .83$) and false positives during “catch trials” (0.5%, $p = .91$), and thus the analyses center on reaction times (RTs). The contrast between tactile and visuotactile RTs demonstrated a clear multisensory facilitation effect (tactile, 383.3 ± 2.9 ms; visuotactile, 354.9 ± 3.5 ms, $t_{49} = 10.32$, $p = 6.85 \times 10^{-14}$). This multisensory facilitation was independently true for both the control ($p = 7.39 \times 10^{-9}$) and ASD ($p = 3.20 \times 10^{-7}$) groups, demonstrating multisensory facilitation during tactile detection also in the clinical group. However, in general, the RTs of individuals with ASD (376.6 ± 2.8 ms) were slower than that of control individuals (340.5 ± 3.1 ms, $p = 1.57 \times 10^{-4}$). Thus, to examine putative space-dependent multisensory effects across groups, we first computed for each participant and visuotactile disparity an index of multisensory facilitation (i.e., VT – T); the more negative this value, the stronger the multisensory effect. For both the neurotypical ($p = .024$) and the ASD ($p = .019$) groups, facilitation in the detection of a tactile target by a co-presented visual stimulus was space dependent, with the effect being most apparent at smaller visuotactile spatial disparities (Figure 1B). Thus, both groups showed a modulation of behavior based on the spatial structure of co-presented visual and tactile stimuli, consistent with the encoding of PPS.

To characterize the PPS effect more fully, we fit RTs to a sigmoidal function (equation 1 in the Supplement) with its central point and slope at the central point as free parameters. After removal of participants with very poor fits (see the Supplement), this function closely fit the pattern of RTs (average R^2, 0.78 ± 0.02, mean ± SEM) and did so equally for the two participant groups ($p = .43$). We equally attempted a linear fit (also with 2 degrees of freedom), but in the current dataset, the sigmoidal fit accounted better for the observed data than a linear fit did (sigmoidal; mean [including poor fits] $R^2 = 0.64$; linear mean $R^2 = 0.53$, $p = 1.012 \times 10^{-11}$).

Although there was a tendency for those with ASD to have a smaller PPS at baseline (individuals with ASD, 32.68 ± 1.64 cm; neurotypical control subjects, 34.09 ± 0.67 cm, $p = .18$, F-test main effect), in the current dataset, this difference failed to reach significance [but see (25,26) for evidence suggesting smaller PPS in ASD than neurotypical individuals]. More importantly, however, to our knowledge, the current report is the first to examine the resizing of PPS in individuals with ASD as a function of an experimental manipulation—the presence of another individual, in this case. In line with Teneggi *et al.* (20), the presence of another individual (social condition) appeared to overall shrink our participants’ PPS (nonsocial, 33.39 ± 0.89 cm; social, 31.46 ± 0.82 cm, $p < .001$, F-test main effect). Critically, this resizing was true in control participants (nonsocial, 34.09 ± 1.64 cm; social, 29.66 ± 1.28 cm, $p = 5.96 \times 10^{-6}$) but not for the ASD group (nonsocial, 32.68 ± 1.67 cm; social, 33.27 ± 1.82 cm, $p = .26$) (Figure 1C) (interaction group × social context, $F_{2,48} = 15.2$, $p < .001$). Similar (but nonparametric owing to their skewed distribution) analyses on the gradient of PPS (parameter b in equation 1 in the Supplement) demonstrated no difference between or within groups (all $p > .25$). The most striking feature of these estimates was their marked variability (see Figure 1D).

Finally, as a confirmatory analysis, we estimated again the central point of the psychometric function describing visuotactile RTs as a function of visuotactile distance via the Spearman-Karber method (27). This method allows for

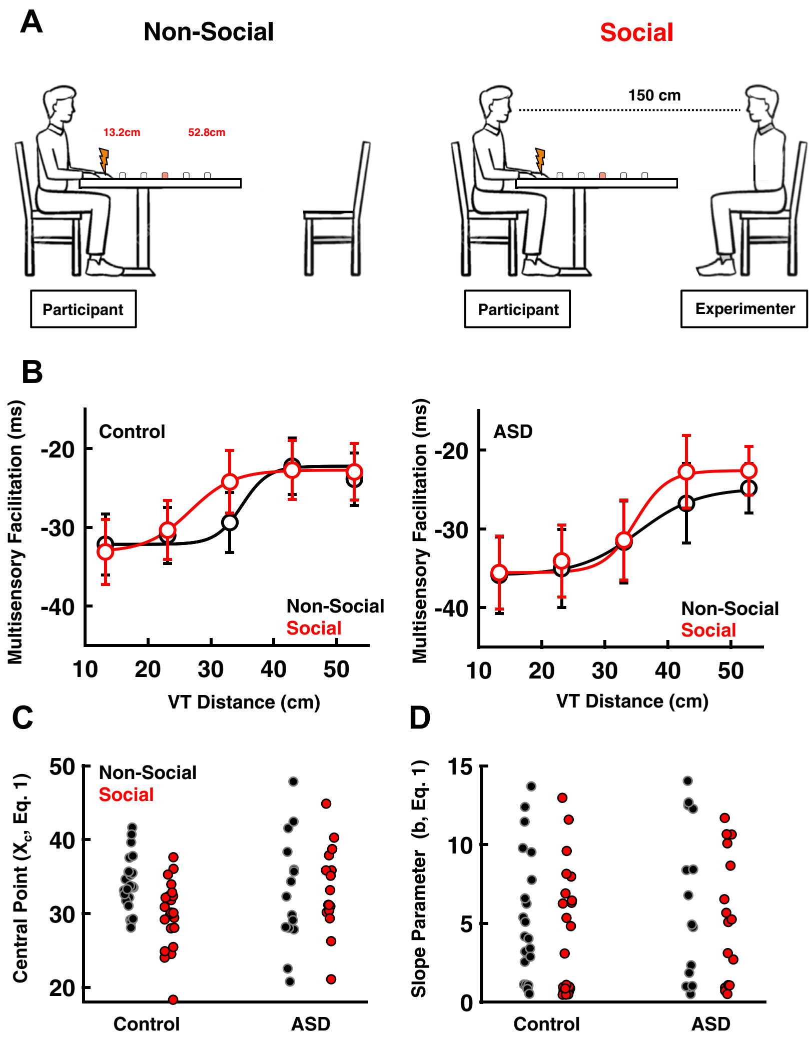

Figure 1. Methods and behavioral results. **(A)** Experimental setup. Participants responded as fast as possible to tactile stimuli (orange), which could be paired with visual stimuli (red, example show at third distance) at different distances (D1–D5, 13.2–52.8 cm). In different blocks, an experimenter would sit facing the participants with a neutral expression (social blocks). In the nonsocial blocks, there was nobody else in the experimental room. **(B)** Visuotactile (VT) reaction times as a function of VT distance. Both for neurotypical control participants (left) and participants with autism spectrum disorder (ASD) (right), reaction times were further facilitated when visual stimuli were near the body, demonstrating a peripersonal space effect. The facilitation was well expressed in the majority of participants by a sigmoidal function in both the nonsocial (black) and social (red) blocks. The fit shown is to the average reaction times across participants, and not the average fit. **(C)** Extracted central point. Peripersonal space becomes smaller in neurotypical control participants (left) but not in participants with ASD (right) during the social blocks. **(D)** Extracted slope parameter. The gradient of tactile reaction times separating peri- and extapersonal space did not change with social context in either group, and instead was characterized by a marked interparticipant variability.

estimating the measures of interest without sigmoidal fitting, and thus we were able to include all participants in this analysis. Results confirmed an interaction between social context and participant group (analysis of variance $F = 6.05$; $p < .01$). This effect was driven by the resizing of PPS within a social setting in the control group (nonsocial: 36.18 ± 1.54 cm; social: 32.72 ± 1.17 cm, $p = .021$), but not in the ASD group (nonsocial: 32.11 ± 1.66 cm; social: 33.71 ± 0.92 cm, $p = .12$).

There was no correlation between ASD symptomatology as measured by the Social Responsiveness Scale and the degree to which PPS size (as measured by the Spearman-Karber method) changed owing to social context (all $p = .17$).

Physiological Marker Suggests Unchanged Multisensory Integration During Social Context in ASD

The behavioral paradigm employed above allows mapping PPS via a task that has been classically used to index multisensory interactions and suggests that while PPS in individuals with ASD may be smaller [empirically supported by (25,26)] and theoretically proposed in (28)], its starker defining characteristic is its inflexibility. In contrast to neurotypical individuals, PPS did not remap for individuals with ASD during a social context. In this behavioral paradigm, however, participants are instructed not to respond to visual stimuli alone. This experimental design choice was driven by the fact that inclusion of "catch, nonresponse" trials greatly reduces the expectation bias that results from having to respond on every trial [see (29,30)]. However, not indexing unisensory visual-only trials impedes ascertaining whether true multisensory integration occurred, via race (31) or drift-diffusion (32) models, both models requiring RTs to every component (e.g., V, T, and VT).

To take a different approach toward assessing true multisensory integration (vs. interactions), we turned to EEG. We sought to assess visuotactile multisensory integration as a function of spatial disparity, social context, and clinical diagnosis. In a first step, we computed evoked (i.e., baseline-corrected, baseline from −200 to 0 ms after stimulus onset) global field power (GFP) (see Supplemental Methods), an index of overall neural response strength. This analysis demonstrated a reliable evoked tactile response beginning at 151 ms after stimulus onset ($p < .01$). This tactile GFP signal peaked at 334 ms after stimulus onset (Figure 2A, leftmost). Visual evoked responses were reliably indexed somewhat later, beginning at 170 ms after stimulus onset ($p < .01$) and peaking shortly thereafter at 182 ms after stimulus onset (Figure 2A, second column). Response to combined visuotactile stimulation began 152 ms after stimulus onset ($p < .01$) and peaked at 218 ms after stimulus onset (Figure 2A, third column). With regard to their spatial distribution on the scalp, the tactile response was characterized by a central positivity (Figure 2B, leftmost), the visual response was characterized by an occipital negativity (Figure 2B, second column), and the visuotactile response was a combination of these topographies, showing both a negativity in posterior electrodes and a positivity pole over frontocentral electrodes (Figure 2B, third column).

To determine whether the presentation of visuotactile stimuli elicited a response indicative of multisensory integration, we created an artificial summed (i.e., visual+tactile) response (the sum occurs at the raw voltage level, and then GFP is extracted from this artificial summed response). An actual multisensory (paired) response that deviates in a superadditive fashion from this linear prediction may be considered a hallmark of multisensory integration [see (33) for a review, and (34,35) for a similar approach within the study of PPS]. However, also see (36,37) for an argument that superadditivity may not index multisensory integration when indexing ensembles of neurons, as opposed to single units. The contrast between the actual and summed GFP demonstrated superadditivity of the multisensory response ($V + T < VT$) between 153 and 175 ms after stimulus onset ($p < .01$). The latency of this effect is fairly late (potentially owing to the fact that we are indexing montage-wide neural strength) yet is in line with our previous EEG [approximately 125–160 ms; see Noel *et al.* (26)] and electrocorticography [approximately 200 ms in the cortex; see Bernasconi *et al.* (34)] characterizations of PPS. At latter latencies (300 ms+), we observed stark subadditivity, likely because of nonlinearities in neural ensemble responses that are not appropriately handled when summing visual and tactile unisensory responses. It is precisely for this reason that we consider super- and not subadditive responses in indexing multisensory integration with EEG.

Importantly, the presence of a superadditive response was true for both control subjects (between 154 and 170 ms after stimuli onset, $p < .01$) and individuals with ASD (between 158 and 174 ms after stimuli onset, $p < .01$), again indicating that the latter group showed normal baseline (i.e., space-independent) multisensory integration (12). While the evoked multisensory response at its peak amplitude was driven by a widespread negativity in posterior electrodes and positivity more anteriorly, the topography of the difference wave was focused with a positivity in centroposterior electrodes (Figure 2B, rightmost; electrodes highlighted in white demonstrate a voltage difference between the paired and summed response).

Having restricted our period of interest to between 158 and 170 ms after stimulus onset (the union of the periods demonstrating a response indicative of multisensory integration in all groups), as well as our spatial window of interest to

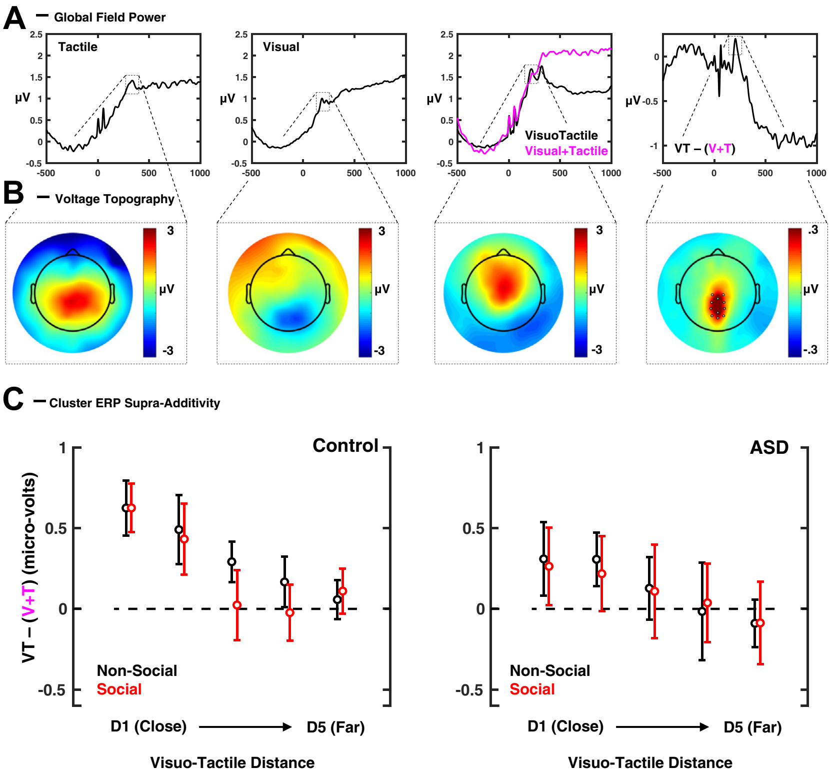

Figure 2. Electroencephalography results. **(A)** Global field power as a function of sensory modality. Results show clear evoked responses for tactile (T) (leftmost), visual (V) (second panel), and visuotactile (VT) (black, third panel) stimuli presentations. More importantly, the VT response shows true multisensory integration, being stronger than the artificially summed V+T response (magenta). Rightmost panel shows the difference wave between the paired and summed response. **(B)** Topography of responses and difference wave (rightmost). The topography of responses (nose at the front) is indicative of T (leftmost), V (second panel), and VT (third panel). The rightmost panel shows that the superadditive multisensory effect is driven by electrodes in centro-occipital areas, between unisensory visual and somatosensory areas. **(C)** Voltages during superadditive period within the cluster driving the global field power effect. The difference in voltage between the paired (VT) and summed (V+T) conditions show a clear multisensory integration effect and one that is dependent on spatial disparity between V and T. Most interestingly, social context (black = nonsocial, red = social) modified the degree of multisensory integration in control subjects (left) but not in individuals with autism spectrum disorder (ASD) (right). ERP, event-related potential.

those centroposterior electrodes driving the multisensory effect (Figure 2B, rightmost), we next investigated whether this response differed based on visuotactile disparity and how it varied as a function of social context and participant group. We extracted and averaged voltages within the spatiotemporal window defined above for each participant, modality type (T, V, or VT), and distance (in the case of V and VT). Note, this corresponds to traditional event-related potential analyses, after having restricted our spatiotemporal region of interest, given the GFP results. We computed the degree of multisensory superadditivity (VT – [V + T], positive values indicating greater multisensory integration) and performed a 5 (distance) by 2 (social context) by 2 (participant group) mixed analysis of variance.

Results demonstrated that the multisensory response was indeed graded by visuotactile disparity (F = 6.02, $p < .001$) (Figure 2C), being strongest when touch and vision were presented near each other and progressively decreasing with distance between them (D1 through D5, respectively; 0.46 ± 0.10 μV, 0.34 ± 0.11 μV, 0.15 ± 0.13 μV, 0.06 ± 0.08 μV, −0.02 ± 0.07 μV). Most importantly, at near distances (D1 and D2, corresponding to 13.2 and 23.1 cm, respectively), this metric had positive values significantly different from zero (all $p < .006$), indicating a true multisensory effect. This effect was present in control subjects (all $p < .01$) and in individuals with ASD, but only for the nearest distance in the latter group (D1, p = .04; D2, p = .12). Thus, while the behavioral results failed to indicate differently sized PPSs in control subjects and those with ASD, the EEG suggests that these two groups do indeed differ in overall size, as demonstrated by previous behavioral studies (25,26).

The main effect differentiating control subjects (0.27 ± 0.12 μV) and individuals with ASD (0.12 ± 0.11 μV) regardless of distance or social context approached but did not reach significance (p = .06), as did the contrast between social contexts regardless of experimental group and distance (p = .13). Thus, also at the level of event-related potential, the current results suggest that individuals with ASD show visuotactile multisensory integration. Critically, however, the group-by-social-context did show a significant interaction (F = 3.74, p = .019). This latter effect was driven by the fact that social context altered the general degree of multisensory integration in neurotypical control subjects (nonsocial, 0.42 ± 0.12 μV; social, 0.14 ± 0.16 μV, p = .014), but not in individuals with ASD (nonsocial, 0.15 ± 0.13 μV; social, 0.14 ± 0.13 μV, p = .83). The three-way interaction was not significant (p = .32), seemingly because of event-related potential modulation by space, and social context was not strong enough in the neurotypical group (p = .043) to drive a three-way interaction. Together, the EEG results show multisensory integration in control subjects and individuals with ASD and show an overall modulation of multisensory integration depending on social context in control subjects but not in individuals with ASD.

Neural Network Modeling: Differences in E/I Balance in Autism May Cause PPS Inflexibility

Having established that both control subjects and individuals with ASD showed a PPS effect behaviorally, as well as the presence of multisensory integration as indexed by physiology (i.e., superadditivity) that was greatest in the near space, we attempted to provide a neural modeling framework capable of accounting for the apparent inflexibility of PPS in individuals with ASD. Note, this is provided as a proof of principle, because a wide array of potential neural implementations is possible [see (38) for the latest neural network model of PPS]. For our purpose, we adapted an existing biologically plausible neural network model of PPS (22–24) by 1) reducing the number of neurons simulated, 2) rendering it deterministic by eliminating noise sources, and 3) introducing a mapping between neural activation and RTs (see Methods and Materials and Figure 3A for details). Importantly, these three ingredients (and the targeted, hypothesis-driven choice of free parameters) allowed us for the first time to use this neural network within the context of a model fitting procedure (39).

First, we fitted the neural network to the psychophysical data from neurotypical individuals under the nonsocial condition. Here, K_1, K_2, α, and Lim (see equation 3 and equation 4 in the Supplement) were allowed to vary while the rest of parameters (see Table S1) were fixed to the values in Magosso *et al.* (22,23). These parameters were chosen given that they bear relation to features that are anatomical and likely immutable across the duration of the experiment but that could account for differences between individual participants. Most importantly for this first fit, results demonstrated that we were able to closely reproduce the pattern of RTs exhibited by healthy control subjects during the nonsocial condition (root-mean-square error [RMSE] = 0.41) (Figure 3B). For the following steps, K_1, K_2, α, and Lim are set to this configuration, which serves as baseline.

Next, we attempted to account for the shrinking of PPS in control individuals during the social context [see findings here and in Teneggi *et al.* (20)]. We entertained two possibilities (although certainly other solutions are possible and were not entertained here). First, we fit the neural network with feedback synaptic weight (parameter, equation 4 in the Supplement) as a free parameter, given that previous reports (22,40) have postulated that changes in the strength of the synapses connecting unisensory and multisensory areas may account for the plastic resizing of PPS. However, the above possibility would require a very quick update in synaptic strengths, and thus we posited that instead, the social context may reshape PPS by directly modulating the gain of the multisensory neuron (parameter r^m, equation 7 in the Supplement). This second potential source of modulation could originate from a number of long-range sources, for example, social cognition structures such as the amygdala or orbitofrontal cortex (41,42), and could be implemented via a number of (quick) functional processes, such as altering the local chemical balance via neuromodulators. Model fits (Figure 3B) showed that the latter was the most likely possibility, with modification of r^m (RMSE = 0.76) providing a better fit than alterations of B_0^v (RMSE = 2.03). Thus, from the possibilities tested here, the resizing of PPS during a social context is most parsimoniously explained by a modulation in the gain of the multisensory neuron.

As a last and most important step, we must explain why a social context—via modulation of r^m—does not remap PPS in ASD. To do so, we assumed that r^m is uncorrupted in ASD and instead considered that the E/I regime imposed by the "Mexican-hat" unisensory connectivity (neurons are laterally

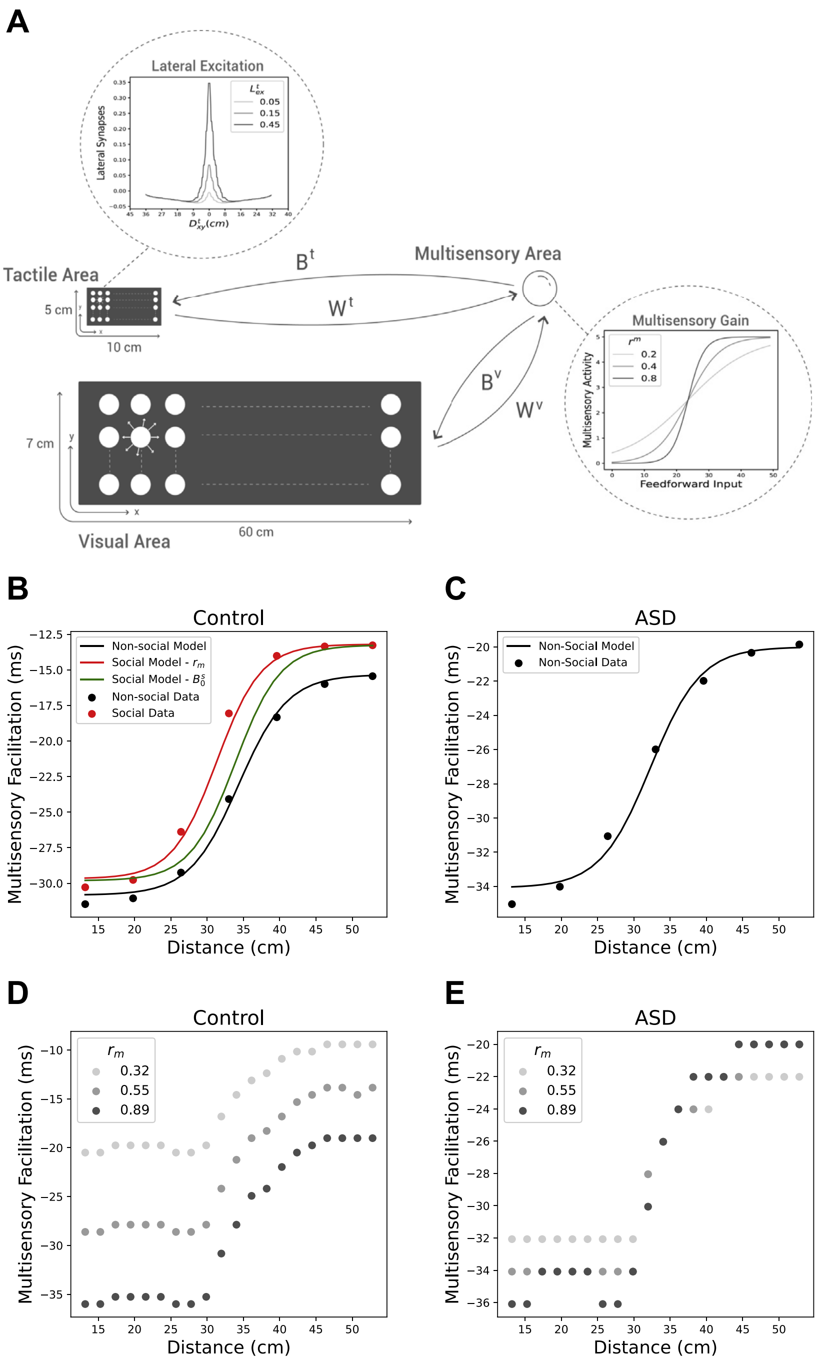

Figure 3. Neural network model. **(A)** Neural architecture. The neural network is composed of a tactile area coding for the hand, a visual area coding for near and far space, and a multisensory neuron receiving projections from the unisensory areas and reciprocally sending feedback projections back to unisensory areas. The output of each neuron is dependent on input-output functions, and the inset on the right shows examples of different gain functions for the multisensory neuron. Within unisensory areas, neurons are laterally connected by a "Mexican-hat" pattern, with near excitation and far inhibition (see inset on the top). **(B)** Model fits to control participants. As a first step, we fit multisensory facilitation (y-axis) in reaction time as a function of distance from the body (x-axis) in the neurotypical control and nonsocial condition (black). Seven distances generated from a sigmoidal with parameters equal to the median experimental parameters were used as observed data. The model is well able to account for observations. Then, we try to explain the impact of the social manipulation by either a change in neural gain at the level of the multisensory neuron (red) or the strength of feedback projects (green). The former approach accounted best for observed data. **(C)** Model fits to individuals with autism spectrum disorder (ASD). The strength of excitatory lateral connections was allowed to vary from the nonsocial control and the nonsocial ASD model, and this manipulation was well able to account for idiosyncrasies in the shape of peripersonal space in ASD (see main text and simulations in Figure S1). **(D)** Impact of multisensory gain under the control excitatory/inhibitory regime. Increasing gain of the multisensory neuron (from light gray to black) increased the size of peripersonal space. **(E)** Impact of multisensory gain under the ASD excitatory/inhibitory regime. Increasing gain of the multisensory neuron (from light gray to black) did not affect the size of peripersonal space.

connected with near excitation and far inhibition—see inset at the top of Figure 3A; equation 2 in the Supplement) may be different in control neurotypical and ASD individuals. Indeed, a substantial literature suggests this possibility (6,7), and simulations showed that increases in L_{ex}^s (i.e., more excitation) led to reductions in the size of PPS (Figure S1). That is, an increase in the relative strength of lateral excitations (vs. inhibition) of connections within unisensory areas, as is hypothesized in ASD and routinely demonstrated in animal models, would lead to smaller PPS, which is what Mul *et al.* (25), and Noel *et al.* (26) have reported, and is numerically (but not statistically) consistent with the findings here. Thus, we let L_{ex}^s be a free parameter and fit the ASD data during the nonsocial condition (starting from the baseline, control nonsocial model). This exercise improved the fit to data from the baseline neural network (RMSE = 0.54) and suggested a fourfold increase (from 0.15 at baseline to 0.63) in E/I ratio from neurotypical individuals to individuals with ASD (Figure 3C). Most importantly, we then examined the potential impact r^m would have under this new E/I regime. As alluded to above, we observed that under the default (control) condition, modulations of r^m are reflected in the size of PPS (Figure 3D). However, under an elevated general state of lateral excitation, r^m had little to no impact on the size of PPS (Figure 3E). In other words, the well-established E/I imbalance present in ASD (6,7) can account for 1) a putative smaller PPS in ASD and 2) a weakening of the social signal related to the presence of another person and thus renders the mapping of PPS inflexible in ASD. As mentioned above, the neural network utilized has many parameters, and thus it is likely that other combinations of parameters could lead to inflexible PPS representations. These results, in turn, must be taken as a proof of principle. However, we consider it at least noteworthy that an altered E/I regime (which is very well established in the rodent literature) may simultaneously lead to a smaller PPS and one that is unaltered by the gain of the multisensory neuron.

DISCUSSION

We used a multisensory task in which touch was applied on the body and visual stimuli were presented at different distances from neurotypical observers and individuals with ASD to map their PPS. PPS became smaller in neurotypical individuals within a social context. In previous work (20), this reduction in PPS during a social condition has been interpreted as "giving space" to an unknown confederate [in Teneggi *et al.* (20), this space then expands as to "include" the confederate after a positive social interaction]. In this study, we additionally describe for the first time the neural correlates of this social remapping of PPS. In line with observations made during intracranial recordings (34), a neurophysiological "signature" of PPS could be seen as evidenced by changes in multisensory integration as a function of distance. Here, we show that this physiological marker of PPS is modulated by social context in neurotypical individuals. More importantly, both the behavioral and electrophysiological measures concurred in suggesting that PPS remapping and changes in multisensory integration due to social context did not occur in individuals with ASD.

The physiological recordings demonstrated superadditivity during multisensory presentations both in neurotypical participants and in individuals with ASD, and similarly, multisensory RT facilitation (independent of space) was evident in both groups. These facts suggest that the basic processes of multisensory integration are intact in individuals with ASD, as recently suggested by behavioral reports focused on computational principles of behavior (12,43). Instead, the results highlight a more specific anomaly: the modulation of multisensory integration, or lack thereof, in ASD via or during a social context. This finding adds to a series of studies emphasizing anomalies in the finer-grained detail of how individuals with ASD integrate information across sensory modalities and adds to it through its emphasis on the spatial domain, as opposed to the much better studied temporal domain (10,11,44–46).

A critical contribution in this report is the ability to perform formal model fitting of a biologically plausible neural network model of PPS. A number of previous reports have suggested potential changes in underlying neural circuitry to account for observed remapping of PPS. For instance, remapping of PPS may occur because of changes in the strength of feedforward/feedback synapses via Hebbian learning (22–24). However, there are a number of other parameters within the current network, in addition to the strength of synapses, that could resize PPS (this criticism equally applies to this work). An alternative candidate (among many others) is the gain of multisensory neurons. Thus, the framing of the neural network of PPS (22,23) under a model-fitting procedure allows contrasting different hypotheses as to the mechanism that most likely supports the remapping of PPS. Here, we find that in neurotypical individuals and during a social context manipulation, out of the different possibilities tested, it is not the strength of long-range synapses that best explains observed changes in the size of PPS (as it may in explaining the effect of tool use on PPS) (24), but instead the gain of multisensory neurons (i.e., the steepness of their input-output relation) (see Figure 3A).

Collectively, our behavioral and electrophysiological results point to PPS and multisensory integration as being immune to social context in ASD. Our neural network model suggests that potential differences between the neurotypical control and ASD groups in regard to PPS resizing may be explained by well-known anomalies in E/I balance (6,7), where the gain mechanism hypothesized to resize PPS is not effective under a regime of heightened excitation.

This framework emphasizing putative changes in E/I balance and its consequence on the flexibility of neural encoding (in this case, of PPS) may conceptually tie together a number of recent observations and theories within the computational study of ASD (i.e., neurophysiological and computational). More precisely, from a neurophysiological standpoint, Rosenberg *et al.* (47) were able to account for a number of perceptual deficits in ASD by postulating an anomaly in divisive normalization. This latter computation is ubiquitous in the central nervous system (48) and in essence amounts to contextualizing all output from a given neural population before affecting downstream targets (i.e., neural output from individual neurons is divided by the activity of a normalizing pool). This divisive normalization account of perceptual anomalies in ASD [see Rosenberg *et al.* (47)] strongly parallels our speculation regarding changes in E/I balance provided by the "Mexican-hat" lateral connections within a neural area. From a more conceptual and computational standpoint rather than neural implementation level, Lieder *et al.* (49) recently used an auditory frequency discrimination task to demonstrate that individuals with ASD showed a slow updating of Bayesian priors (i.e., expectations). Similarly, Lawson *et al.* (50) suggested that adults with ASD overestimate the volatility of their sensory environment and thus are slower in updating Bayesian priors when confronted with statistically unlikely events. In this vein, Noel *et al.* (51) suggested that PPS is best conceived as a visuoproprioceptive prior, the space where visual stimuli are expected to co-occur with somatosensory input. Thus, previous research has emphasized both anomalies in E/I balance and how this could affect perceptual phenomena and, in addition, has emphasized the slow updating of expectations. Putting it all together, the current findings suggest that the inflexibility in updating neural representations [as in Bayesian accounts (49–51)] may be due to altered E/I regimes or differences in divisive normalization [as in Rosenberg *et al.* (47)] and neural implementation accounts.

Conclusions

To conclude, we attempted to link social and sensory differences in ASD and to add to the rapidly expanding field of computational psychiatry. We showed via behavior and physiology that PPS updating is inflexible in ASD, which is reminiscent of Bayesian accounts suggesting a reduced flexibility of priors (49,50). In addition, we suggested a potential mechanism for this reduced flexibility—ineffective gain modulation within the E/I regime that has been described in ASD (6,7). Broadly, given the role of PPS in bodily self-consciousness (16), these results may recast ASD as a disorder of the self—as it was originally described (52)—and suggest how we may bridge implementation and computational levels of description within the ASD pathology.

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