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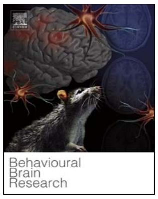

Research report

Socially induced plasticity in sensorimotor gating in the African cichlid fish *Astatotilapia burtoni*

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ABSTRACT

Deficits in prepulse inhibition (PPI), social defeat and social withdrawal are hallmark features of several neurological and neuropsychiatric disorders. However, the link between social environment and PPI i.e., the possible role of social defeat in driving PPI plasticity, is far from clear. Here we explored these questions in the African cichlid fish *Astatotilapia burtoni*, where males exist as two distinct yet reversible phenotypes. In fish communities, DOMs exhibit frequent aggressive and territorial behaviors, threatening and attacking SUBs, which respond either by engaging in fights and fleeing, or by avoiding interaction with DOMs altogether. Social phenotypes were selected using focal observations of dominant and submissive behaviors. Tests of auditory PPI showed markedly decreased PPI in SUBs as compared to DOMs at prepulse/pulse interstimulus interval of ISI 50 ms. Interestingly, further analysis showed the PPI reduction in SUBs was driven by males with low social interactivity. Testing males before and after social transitions revealed increasing and decreasing PPI in ascending and descending males, respectively. In an open field paradigm, SUBs also showed higher levels of wall hugging (thigmotaxis) and freezing when compared to DOMs i.e., an increase in anxiety-related behavior. Together the results suggest distinct yet reversible behavioral PPI phenotypes in *A. burtoni* males, and that social defeat drives PPI plasticity. The fact that PPI deficits are readily reversible by status change implies PPI plasticity may reflect an adaptive response to challenges in the social environment.

1. Introduction

Prepulse inhibition (PPI) is understood as a sensorimotor gating phenomenon regulating sensory flow during early stages of information processing [1,2]. Conceptually, PPI is based on the 'protection of information' theory by Graham [2], describing early information processing is vulnerable to disruption by subsequent sensory stimulation; PPI thus serves as a protective inhibitory mechanism. PPI is typically associated with a sensory (prepulse) evoked attenuation of the startle-reflex in rodents and the eye blink-reflex in humans [1,3,4], but has been also investigated in various other species e.g., fish: [5–9]; bird: [10]; mollusk: [11–13]. The fact that PPI can be assessed across taxa using similar stimuli emphasizes its value for comparative studies of information processing in the CNS. Proper PPI depends on a delicate balance of excitation and inhibition. As such, PPI has proven remarkably sensitive to factors affecting neurotransmitter/modulator levels and physiological state (e.g. anxiety, stress) and PPI deficits are implicated in a range of neurological and psychiatric disorders such as Tourette syndrome and schizophrenia [14–18]. Using pharmacological and genetic manipulations of PPI circuits, significant progress has been made in establishing important pharmacological links between PPI deficits and distinct disorders [14,17,19–24]. However, little is known about the biological context in which alterations in PPI may occur naturally. Thus, manipulation of the social environment, i.e., social isolation and social defeat, has shown great promise in inducing disruption of PPI [25–27]. Similarly, our studies in the African cichlid fish *Astatotilapia burtoni* (*A. burtoni)* showed we can reliably elicit startle plasticity in this species through manipulations of the social environment [28,29]. Here we asked if changes in the social environment also cause differences in PPI.

In most teleost fish, startle is controlled by a pair of large reticulospinal neurons, the Mauthner cell (M-cells) and their associated excitatory and inhibitory networks [30,31]. The M-cells receive multimodal inputs, most notably from the acoustico-lateralis and visual systems and a single action potential (AP) in one M-cell activates contralateral spinal motor networks causing a fast (9–11 ms) body-bend

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(C-start) away from a potential threat [32–34]. Importantly, the one-to-one relationship between an AP fired in one M-cell and the initiation of the C-start behavior provides a causal link between M-cell excitability and behavioral responsiveness [8,35].

A. burtoni is a well-established model system for investigating the influence of social rank on behavior and the underlying endocrine and cellular processes in the brain [36–42]. Males in this species reversibly transition between subordinate (SUB) and dominant (DOM) social status, which is driven by social context and growth [37,38,43–45]. SUBs are pale, reproductively suppressed and exhibit submissive behaviors, while DOMs are brightly colored (blue or yellow), reproductively active, and vigorously defend a territory [44,45]. In social communities, dominant and submissive behaviors can be readily quantified and social transitions can be induced [46–49]. Indeed, threat displays and agonistic behaviors are key components necessary for establishing dominance in *A. burtoni* and have been shown to be a potent social stressor for SUBs [50]. Importantly, in various species subordinate status and social defeat leads to changes in information processing related to the assessment of potential threats e.g., rodents: [51]; crayfish: [52,53], including disruption of PPI [25,26]. Accordingly, we hypothesized that SUBs will show reduced PPI and increased anxiety levels as compared to DOMs, and that a switch from SUB to DOM status reverses behavioral PPI deficits.

2. Methods

2.1. Subjects

Laboratory-raised adult African cichlid fish *Astatotilapia burtoni* were maintained in community holding tanks as previously described [29]. In short, seven communities consisting of 8–12 males and 8–12 females were each housed in an acrylic tank (30 × 30 × 60 cm). Crushed coral gravel was provided as substrate, faux plants provided shelter, and 4–6 terracotta pots served as territories. Standard water conditions (27 ± 1 °C, pH 8.5 ± 0.5) were maintained by a flow-through supply water system. Ambient light was set on a 12 h light/dark cycle. Fish were fed daily using a standard cichlid diet. Experimental protocols were in accordance with relevant regulations and approved protocols of the Hunter College of the City University of New York.

2.2. Social behavior

To quantify social behaviors of *A. burtoni* males in community holding tanks we used a focal observation ethogram modified after [44]. Each male in a community was observed for 10 min twice per week for up to 8 weeks. In each observation session the Dominance Index (DI) [54,55] was calculated for an individual male from the sum of dominant behaviors (chase/bite/threat display/carousel fight, court/mate) minus the submissive behavior ‘flee’. The mean DI of all observations for a given male was used for data analysis. Using the same observations scores (excluding reproductive behaviors) we also calculated the Conflict Index (CI), which is the total count of all antagonistic interactions between males [56]. As such, the CI emphasizes the number of antagonistic interactions regardless of outcome (i.e., win or lose). For analysis, individuals were ranked by their CI scores and categorized into low, medium and high CI groups.

2.3. Experiment I: prepulse inhibition

The experiments used previously described methods [8,29]. Males (N = 34) were selected from seven community holding tanks and either categorized as SUBs (N = 20) and DOMs (N = 14), or as low (N = 11), medium (N = 12), and high (N = 11) CI males. Individual males were carefully transferred to the experimental tank using a small container. The circular acrylic experimental tank (76 cm diameter, 20 cm height) was situated on an anti-vibration table to eliminate mechanosensory cues and filled with aerated water matching the water conditions of the community holding tank. Between experiments, the experimental tank was emptied and wiped with 50% ethanol. To reduce external cues, the tank wall was opaque and surrounded by a black curtain. A black mesh net confined a circular area (30 cm diameter, 18 cm height) in the center of the tank where the fish swam freely for a 30 min acclimation period.

Startle escape responses i.e., C-starts were evoked by high sound pips (200 Hz single sine wave; 166 or 172 dB, in water re. 1 μPa) either presented alone (pulse-only; 7 trials), or in combination with a preceding sound prepulse of lower intensity (140 or 142 dB, in water re. 1 μPa) at prepulse/pulse interstimulus intervals (ISIs) of 50 ms and 200 ms (8 trials). The sound intensities for the startling pulse stimulus represented the mid-range of a stimulus/response curve previously established for *A. burtoni* [29]. The time between trials (2–15 min) and the presentation sequence of pulse-only and prepulse/pulse stimuli varied randomly to avoid habituation (see [8,29]). Sound pips were created in Igor Pro (WaveMetrics, Portland, OR), amplified via a Servo 120A power amplifier (Samson, Hicksville, NY), and produced by either of two UW-30 underwater loudspeakers (University Sound, Buchanan, MI) located on opposite sides in the tank. Escapes were recorded at 1000 frames per second using a high-speed video camera (resolution 800 × 600 px; i-Speed 2 Olympus, Tokyo, Japan) and digitally stored. The startle escape response in fish i.e., C-start is an all-or-none response evoked by a single action potential in one of two Mauthner neurons [32,34]. For analysis we either used the individual binary startle/no startle response ratios or the more common PPI effect based on the response/trial probability for pulse-only and the two PPI stimulus conditions. The prepulse effect was defined as

$$100 - \left(\frac{\textit{response to prepulse}}{\textit{response to pulse only}} \times 100\right).$$

Some fish showed prepulse facilitation (PPF) i.e., overall larger response probabilities to the prepulse/pulse stimulus than to the pulse only stimulus. In these cases, the formula was modified to

$$\left(100 - \left(\frac{\textit{response to pulse only}}{\textit{response to prepulse}} \times 100\right)\right) \times -1$$

to ensure symmetrical PPI (positive) and PPF (negative) effect values for statistical comparisons.

2.4. Experiment II: prepulse inhibition before and after social status reversal

In this separate experiment we asked if the magnitude of PPI responses change in males undergoing social transition. Therefore, males (N = 17) were tested before and after social transition either ascending to or descending from DOM status in three subsequent experimental sessions. Males which did not change status were used as controls. Social transitions were stimulated by removing or adding males of different size from or to a community [49]. Fish were only used after status change remained stable for at least three weeks as established by focal observations (see above). Since transition times differed for individual males the time between experiments varied with a mean time of 115 days ± 47 SD and 83 days ± 52 SD days between sessions 1–2, and 2–3, respectively.

2.5. Experiment III: open field behavior

A different set of A. burtoni males (N = 31) from seven community holding tanks were tested in an open field paradigm to assess activity and anxiety-related behaviors. Individuals were transferred using a small container and carefully released into the center of an opaque circular acrylic tank (30 cm diameter, 18 cm water height) filled with aerated conditioned water (27 ± 1 °C temperature) and surrounded by a black curtain to minimize external visual cues. Between experiments, the experimental tank was emptied and wiped with 50% ethanol. Ventral views of the freely swimming fish were recorded using a video camera (30 fps, resolution 800 × 600 px; i-Speed 2 Olympus, Tokyo, Japan). A period of 30 min was recorded and the last 15 min were analyzed using video tracking software (BIOBSERVE, demo version 3.0.1.255). Analysis parameters included total distance traveled (normalized to body length), freezing duration (defined as proportion of time spent with complete cessation of movements) and, time spent in the center zone of the arena. For the latter, a virtual circular zone was defined as one standard body length of the fish away from wall.

2.6. Statistical analysis

Data were analyzed in R Statistics (version 3.3.2) using the *geepack* package for generalized estimating equations (GEE) and the *ImPerm* package for permutation tests, and graphed in Kalaidagraph (version 4.1.3). Boxplots were used for side-by-side comparison of several samples. Mean values and ± standard deviations (SD) are reported in the text to supplement information of box plots. Datasets were tested for assumptions of normality. To analyze startle/no-startle ratios in pulse-only and PPI stimulus conditions (see above) we used a repeated measures GEEs with a logit link function and binomial variance function, which is appropriate because it considers the dependence and hierarchical structure of the datasets. Hypotheses concerning regression parameters in the GEE were tested using Wald chi-square statistics. Means of PPI effects and open field behavior were analyzed using permutation tests, which are appropriate for small samples from unknown distributions. Benjamini-Hochberg correction was performed on the resulting *p*-values for all multiple comparisons to control for the expected proportion of false discoveries [57].

3. Results

3.1. Experiment I: prepulse inhibition

To characterize baseline PPI in SUBs and DOMs we first conducted a within status comparison of their binary response ratios (startle/no startle) in the pulse-only and the two prepulse/pulse conditions (ISI 50 and ISI 200 ms). The results indicate in DOMs (N = 14) a substantial decrease in response ratio in both prepulse conditions i.e., PPI (GEE, adjusted: ISI 50 ms: $p = 0.002$; ISI 200 ms: $p = 0.012$; Fig. 1A, right). In contrast, SUBs (N = 20) showed a small drop in response ratio for both prepulse conditions however, this reduction was not significant (Fig. 1A, left).

An alternative analysis of the same data set was performed based on the CI scores (see Methods Section 2.2). In a social community, DOMs are clearly the most active males frequently threatening and chasing SUBs. Interestingly, however, SUBs either engage in fights and eventually flee or avoid conflict interactions with DOMs altogether. These behavioral traits can be distinguished using the Conflict Index (CI), which reflects the sum of all conflict related behaviors towards other males performed by an individual male [56]. Accordingly, males were ranked by CI and subdivided for analysis into low, medium and high CI interactive males. Males with the most interactions (high CI) are DOMs and males with low and medium interactions are essentially SUBs [56]. Fig. 1B shows the within comparisons of response ratios between pulse-only and PPI stimulus conditions for the three groups. Significant reductions were found in response ratios of high CI males (N = 11) in both PPI conditions (GEE, adjusted: ISI 50 ms: $p < 0.001$; ISI 200 ms: $p = 0.002$) and of medium CI males (N = 12) at ISI 50 ms (GEE, adjusted: ISI 50 ms: $p = 0.036$), whereas the low CI group (N = 11) showed no significant difference in response ratios between stimulus conditions.

To compare PPI between the social groups we calculated the PPI effect for both ISIs (i.e., the percent change of startle probability in prepulse/pulse and pulse-only stimulus conditions; see Methods Section 2.3 for details). Fig. 2A implies lower PPI effect in SUBs (N = 20) for both ISIs (ISI 50 ms: mean 26.3% ± 66.8 SD; ISI 200 ms: mean 15.6% ± 62.5 SD) as compared to DOMs (ISI 50 ms: mean 70.9% ± 43.8 SD; ISI 200 ms: mean 51.6% ± 44.5 SD; N = 14). However, statistical testing revealed a significant difference only for ISI 50 (permutation test: $p = 0.025$; Fig. 2A, two left boxes).

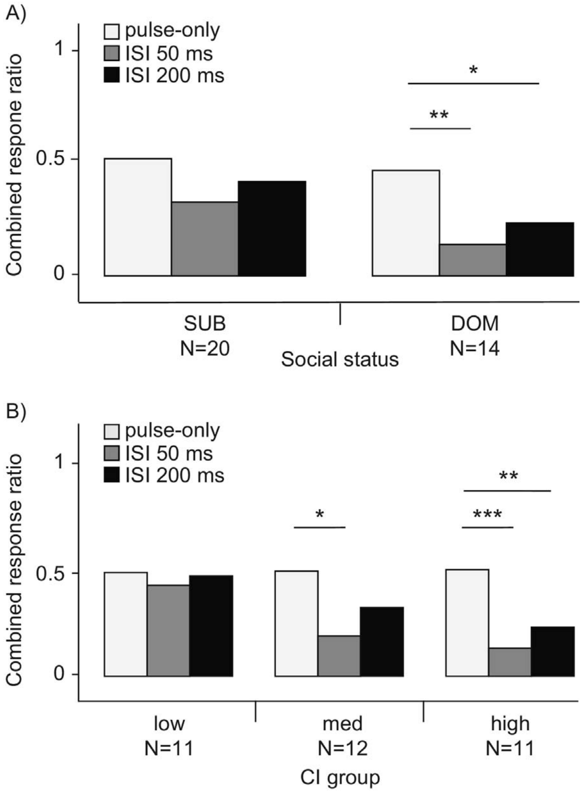

Fig. 1. Binary startle/no-startle response ratios of social groups. Plots of combined response ratios during pulse-only and the two prepulse-pulse stimulus conditions (ISI 50 and 200 ms) in (A) SUBs and DOMs, and (B) males with low, medium, and high conflict index (CI). Note: data in A and B involve the same individuals with different social categorization. (* p = 0.012; ** p = 0.002).

Again, dividing males in three CI groups crystallized these differences in PPI further. Fig. 2 B reveals different PPI effects between the low (N = 11) and high CI groups (N = 11) for ISI 50 (low CI: mean 11.6% ± 67.6 SD *vs*. high CI: mean 70.3% ± 40.7 SD; permutation test $p = 0.025$) and ISI 200 (low CI: mean 1.9% ± 59.0 SD *vs*. high CI: mean 55.1% ± 40.0 SD; permutation test: $p = 0.025$). Males in the medium CI group appear to show PPI effects (ISI 50 ms: mean 51.5% ± 63.3 SD; ISI 200 ms: mean 34.0% ± 63.1 SD; N = 12) comparable to DOMs, however, differences between medium and low CI males were non-significant (Fig. 2B, light grey boxes).

Given that differences in binary startle ratios in response to pulse-only stimuli were not significant between the social types (compare light gray bars in Fig. 1A) the results suggest that the observed reductions of PPI in SUBs or low CI males are not driven by difference in baseline excitability, but by transiently reduced inhibitory input during PPI. However, due to lack of power, we were unable to conclude statistical equivalence of startle ratios under a reasonable threshold.

3.2. Experiment II: prepulse inhibition before and after social status reversal

Our results thus far show a relationship between social defeat and low levels of PPI. To assess if changes in social status can indeed drive changes in PPI we performed a separate experiment where males were tested for PPI before and after undergoing a social transition. Indeed,

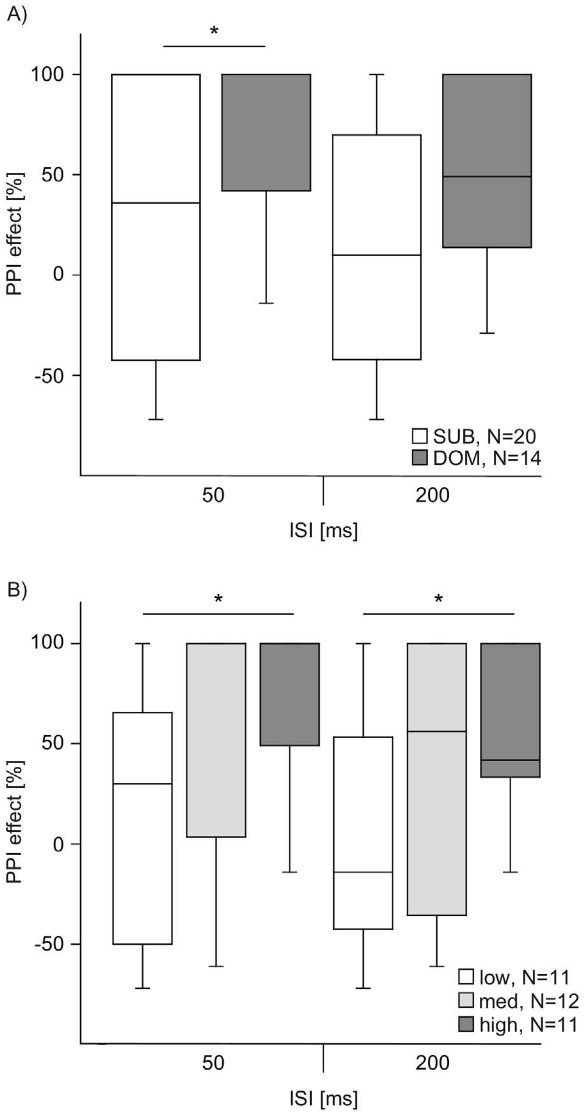

Fig. 2. PPI effects of social groups. Boxplots of calculated PPI effect for prepulse-pulse ISI 50 and 200 ms stimulus conditions in (A) SUBs and DOMs and (B) males with low, medium and high conflict index (CI). Note: data in A and B involve the same individuals with different social categorization. (* p = 0.025).

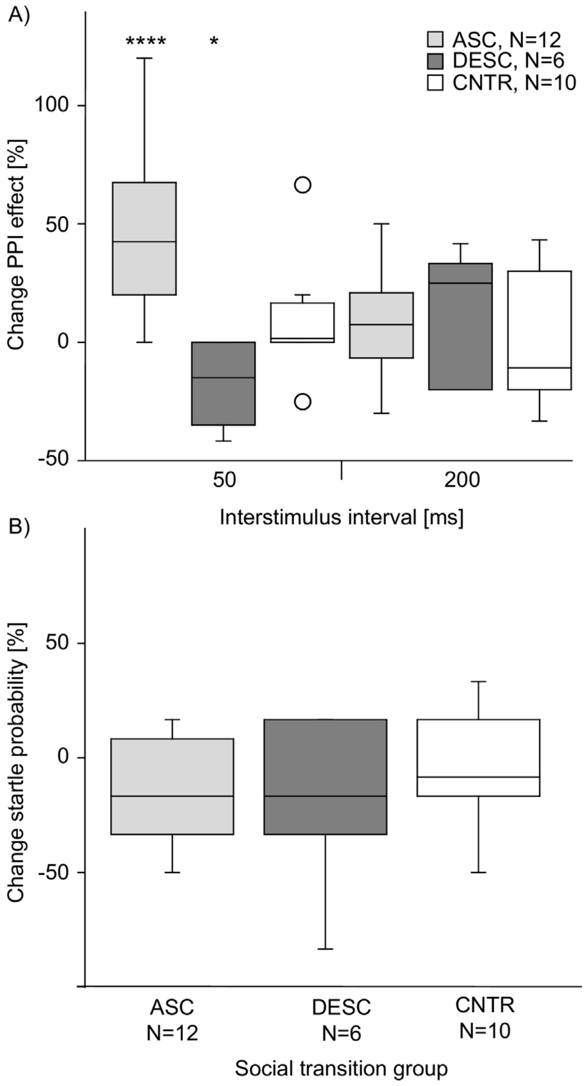

Fig. 3. PPI plasticity during status change.
(A) Boxplots indicating change in PPI effect at the two prepulse-pulse stimulus conditions (ISI 50 and 200 ms) measured before and after status transition for ascending (ASC), descending (DESC) and males not undergoing a social transition (CNTR). (* p = 0.016; **** p < 0.001). (B) Boxplots of the change in startle probability in response to pulse-only trials for the three social transition groups.

social transitions occur in this species naturally (see Introduction), or can be triggered by changing the make-up of the social communities (see Methods Section 2.4). Specifically, we hypothesized that males ascending to or descending from DOM status will show corresponding increase and decrease in PPI, respectively. Therefore, we calculated the change in PPI in ascending (N = 12) and descending (N = 6) males and in males which did not change status (N = 10), and compared the means in the different groups to a hypothetical value of zero. Indeed, Fig. 3A illustrates an increased PPI effect for ISI 50 ms in ascending males (GEE, adjusted: $p < 0.001$), and a decreased PPI effect in descending males (GEE, adjusted: $p = 0.016$). In controls i.e., males not undergoing social transition, PPI remained unchanged (Fig. 3A, white boxes). No obvious change in PPI effect was found at ISI 200 ms for any of the transitioning males (Fig. 3A, box plot on the right). Due to the relatively small sample size we did not further subdivide the males into CI groups.

Given that these experiments involved testing males repeatedly in subsequent sessions we also examined baseline startle, i.e. escapes in response to pulse-only stimuli. Fig. 3B shows the mean change in baseline startle probability between sessions for the three groups. The results imply an overall reduction in startle (GEE, adjusted: ASC: $p = 0.014$, DESC: $p = 0.16$, CNTR: $p = 0.65$). However, no significant differences in baseline startle probability between the groups were found ($p = 0.345$).

3.3. *Experiment III: open field behavior*

One possible cause for the observed reduced PPI in SUBs (and low CI males) might be anxiety in response to repeated social defeat. Therefore, we tested a different set of males (N = 31) in an open field paradigm and compared swimming activity and anxiety-related behaviors (see Methods Section 2.5 for details).

Fig. 4A illustrates representative swimming trajectories for SUBs and DOMs, indicating differences in both activity and wall hugging (thigmotaxis). The quantification of these different measures for DI and CI categorizations of males are presented in Figs. 4B-D in the left and right box plots, respectively. Results imply a decrease in total distance traveled in SUBs (mean 72.4 bl ± 37.3 SD; N = 13) as compared to DOMs (mean 108.1 bl ± 54.9 SD; N = 18; Fig. 4B, left). However, the difference did not reach significance (One-way ANOVA with permutation test: $p = 0.072$). Similarly, no overall significant difference (One-

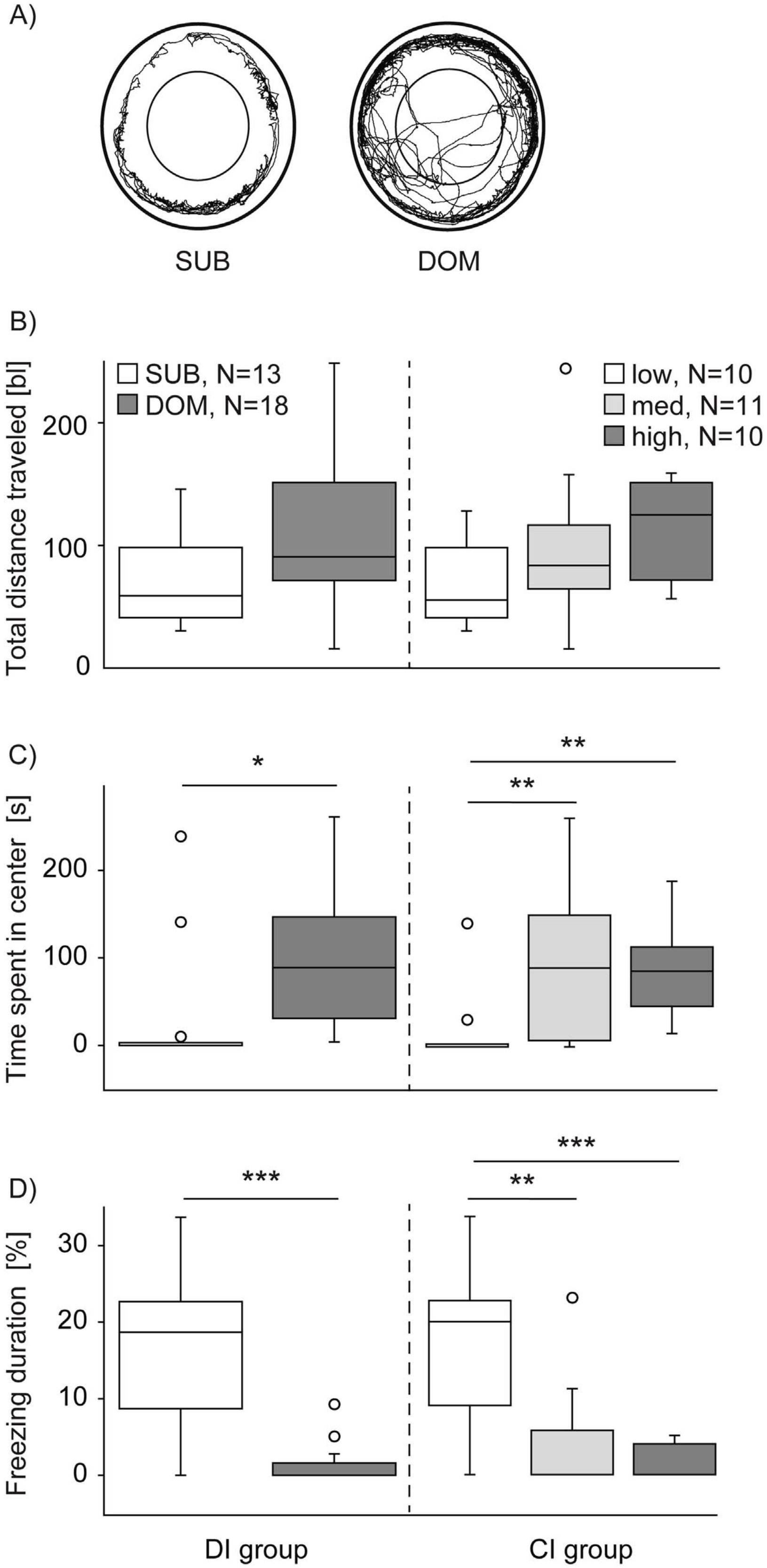

Fig. 4. Activity and anxiety-related behaviors in social groups. (A) Representative swimming trajectories (15 min) for SUBs and DOMs. (B–D) Boxplots showing total distance traveled (B), total time spent in the center of the arena (C), and freezing duration (D) for SUBs and DOMs (left) and males with low, medium and high CI (right). Time spent in the center: * $p = 0.025$ (left), ** $p = 0.018$ (right); Freezing: *** $p < 0.001$ (left), ** $p = 0.003$, *** $p < 0.001$ (right).

way ANOVA with permutation test: $p = 0.075$) was found for CI categorization of males in low (mean 66.8 bl ± 33.1 SD; N = 10) as compared to medium (mean 97.3 bl ± 64.9 SD; N = 11) and to high CI groups (mean 115.0 bl ± 38.7 SD; N = 10; Fig. 4B, right).

In contrast, SUBs clearly spent less time in the center of the arena (i.e., thigmotaxis) as compared to DOMs (SUBs: mean 30.3 s ± 73.3 SD; N = 13 vs. DOMs: mean 98.1 s ± 66.2 SD; N = 18; One-way ANOVA with permutation test: $p = 0.025$).

We also found an overall effect of CI for this measure (One-way ANOVA with permutation test: $p = 0.012$). Pairwise comparisons showed that low CI males stand out by spending less time in the center of the arena (mean 17.5 s ± 44.5 SD; N = 10) as compared to medium CI (mean 102.1 s ± 94.4 SD; N = 11) and high CI males (mean 86.1 s ± 53.9 SD; N = 10; Fig. 4C, right).

Fig. 4D (left) illustrates significantly increased freezing behavior in SUBs (mean 16.0% ± 10.8 SD; N = 13) as compared to DOMs (mean 1.7% ± 2.6 SD; N = 18; One-way ANOVA with permutation test: $p < 0.001$). For CI, the results indicate an overall effect (One-way ANOVA with permutation test: $p < 0.001$). Pairwise comparisons showed again that low CI males are distinct showing more freezing (mean 17.4% ± 10.6 SD; N = 10) as compared to medium CI (mean 4.3% ± 7.4 SD; N = 11) and high CI males (mean 1.6% ± 2.2 SD; N = 10; Fig. 4D, right).

4. Discussion

The present study suggests distinct yet reversible behavioral PPI phenotypes in *A. burtoni* males. This notion is supported by two key results: first, SUBs i.e., socially defeated males show substantial attenuations in PPI, and second, changes in status of individual males are accompanied by corresponding changes in PPI. Together, the results imply that the observed PPI plasticity might reflect an adaptation to the social environment.

4.1. Social defeat and PPI

Evidence for environmentally (socially) induced plasticity in sensorimotor gating is established in various rodent models suggesting that social stressors are important modulators of PPI [25–27,58,59]. For example, the isolation-rearing model demonstrates PPI deficits in rodents, but outcomes vary among strains [60–62]. Also, Adamico et al. [26] found that mice repeatedly exposed to short aggressive encounters in a resident-intruder paradigm show reduced PPI and increased anxiety-related behaviors. However, such PPI deficits are not apparent if the intruder is housed in a small group rather than by itself. The latter is in line with other studies showing socially enriched housing conditions can counteract the effect of social defeat on physiology and behavior [59,63]. Thus, the relationship between social defeat and PPI reduction are complex and modifiable by coping mechanisms. Our results in *A. burtoni* are qualitatively comparable with the above studies. However, the PPI deficits we observed in SUBs were more substantial when compared to the rodent studies. Specifically, some SUBs (i.e., low CI males, see below) showed no PPI at all, but rather prepulse facilitation i.e., more, instead of less, startles in prepulse/pulse trials relative to pulse-only trials. A previous study implied that SUBs with low CI are descending and SUBs with medium CI are ascending males [56]. Thus, one possible reason for such large PPI reductions is that the separation of SUBs into low and intermediate CI groups emphasized the PPI effects. In these communities of up to 24 fish, typically 3–4 DOMs emerge vigorously defending territories against challengers and frequently threatening and chasing SUBs across the habitat throughout the day (an average of 18 aggressive behaviors expressed by DOMs within a 10 min observation period). SUBs may avoid injury by fleeing and shoaling with females. Also, the aggression of DOMs is typically directed towards multiple males. Nevertheless, the ‘naturalistic’ social context used here provided for repeated social defeat in SUBs over an extended period, which putatively enhanced the evoked physiological and behavior consequences. Indeed, several studies indicate increased blood cortisol levels in SUBs, suggesting that social defeat raises stress levels in *A. burtoni* males [50,64,65]; see also [46,66]. Consistent with those findings, we found here that SUBs showed increased anxiety-related behaviors in an open field paradigm. Indeed, the latter has been shown to be a promising tool for behavioral screens of anxiety [67,68]. Thus, together with the reduction in PPI, SUBs show two different behaviors linking social defeat to a distinct phenotype in *A. burtoni*.

In this context it is interesting that the categorization of males using the Conflict Index (CI) revealed PPI reductions and increased anxiety-related behavior only in low CI males, i.e., males that avoided agonistic encounters, defined as prototypical SUBs [56]. In contrast, medium CI males, which engaged in fights but eventually flee showed PPI and anxiety behaviors similar to high CI males i.e., prototypical DOMs. These results imply that social defeat has less if any effect on ‘proactive’ medium CI males. In other words, differential coping mechanisms for social defeat exist in *A. burtoni* that seem to predict PPI magnitude. Indeed, in rodents resisting to agonistic encounters appears to diminish or counteract the effect of social defeat as a stressor [59,69].

A recent study selected rats for low and high PPI, which subsequently demonstrated decreased and increased social interactivity, respectively [70]. The authors concluded that PPI drives these differences in social behavior. The present study shows conceptually similar results i.e., a relationship between social interactivity and PPI. The fact that social status transitions in individual males let to corresponding changes in PPI (Fig. 3) suggests that in *A. burtoni* the social environment drives PPI plasticity.

4.2. Possible mechanism for socially induced PPI plasticity

As noted, social defeat is a putative cause for the observed plasticity in PPI and anxiety-related behaviors. One candidate neuromodulator mediating these changes is dopamine (DA). Indeed, social defeat and stress increases extracellular dopamine levels and DA2 receptor activation in rodents [71,72], although the interaction appears to be complex [73,74]. Dopaminergic systems appear to be highly conserved in the vertebrate brain, which includes *A. burtoni* [75]. DA receptor agonists disrupt behavioral PPI of Mauthner cell (M-cell) mediated startles in zebra fish [9]. Moreover, our electrophysiological studies in goldfish demonstrated disruption of PPI using DA agonists by transiently increasing M-cell input resistance following a prepulse with a 50–100 ms lead-time [76,77]. In the present study, SUBs showed PPI reductions most prominently at a prepulse/pulse interval of 50 ms (Fig. 1A and B) i.e., at a time interval where DA modulates M-cell PPI. The latter provides an intriguing, albeit hypothetical suggestion that dopamine might mediate socially induced PPI plasticity.

Serotonin (5-HT) is another possible modulator of the observed PPI plasticity based on the fact that Ketanserin, a non-selective 5-HT$_2$ receptor antagonist differentially affects M-cell feedforward inhibition in SUB and DOM *A. burtoni* males [28]. In rats, 5-HT uptake inhibitors have differential effects on PPI in subordinate and dominant males [58]. However, results in goldfish suggest that 5-HT affects M-cell PPI indirectly by changing the overall excitability in the startle circuit rather than affecting the PPI inhibitory network itself [7].

The present study did not find significant differences in baseline startle ratios between DOMs and SUBs or among the different CI groups. This finding appears to contradict an earlier study using a startle-only paradigm (i.e., no intermixed PPI trials) where we observed higher startle probabilities in DOMs [29]. However, recent experiments indicate that baseline startle in DOMs are affected by a color polymorphism. Specifically, yellow DOMs exhibit higher baseline startle probabilities than blue DOMs, which might be an adaptation to a higher conspicuousness of yellow-pigmented males to predators (unpublished results; [78]). Here we used a mixed population of blue and yellow

DOMs to negate possible confounding effects on baseline startle ratios for the comparison of PPI in SUBs and DOMs.

4.3. *A functional role of PPI plasticity in A. burtoni?*

As noted, one proposed role of PPI is reducing sensory information flow to the central nervous system while preceding information is processed [1,2]. PPI can be conceptualized, at least partly, as an attentional process influencing early stages of information processing [79–83]. Indeed, humans show increased PPI for an attended prepulse [82,84–86]. Similarly, in rodents increasing prepulse salience increases PPI, and the magnitude of PPI correlates to performance in attention discrimination tasks [87]. Thus, reductions in PPI might reflect a shift in attentional focus and/or increased distractibility [88,89]. In other words, processes underlying attention may play also a role in modulating PPI. Applied to *A. burtoni,* the high and low levels of PPI may therefore reflect task-oriented focused attention on competitors in DOMs vs. broad spatial awareness/attention to potential threats in SUBs. Acute awareness of the social environment and an attentional hierarchy has been described in this species [36,90]. As such, the different yet reversible levels of PPI observed in males can be understood as an adaptation to the demands of the social environment.

4.4. *Conclusion*

The goal of the study was to investigate links between chronic social defeat and sensorimotor gating abilities in a naturalistic context. Our results support the notion that only SUBs with an apparent reactive coping style not only show clear behavioral markers of increased anxiety-related behavior but also a disruption of PPI, i.e., a shift in sensory gating ability. The plasticity of PPI in individual males during status transitions makes a compelling argument that changes in PPI might be adaptive. Together the results might enhance our understanding of the biological function of PPI plasticity with potential implications for the interpretation of PPI deficits in other species.

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