

Pizarro, M.^{1,2,.}, Gierke, C.^{1,2,3,5,.}, Díaz, R.^{1,2,6,.}, Palma, J.^{1,2,.}, Iturriaga V.^{1,2,7,.}, Valderrama, A.^{1,2,4,.}, Morales, M.^{1,2,.}, Cabrera, F.^{1,2,4,.}, Leyton, B.^{1,2,4,.}, Roman,Y.^{1,2,4,.} & Del Pino, F.^{1,2}

¹Social Isolation Research Center (SIRC), ²ISOFLY Lab, NiBG, Instituto de Ciencias Biomedicas (ICBM) Fac. de Medicina, Universidad de Chile ³Hospital Clínico Universidad de Chile (HCUCH), ⁴Escuela de Psicología, Universidad Católica Silva Henríquez ⁵Escuela de Psicología, Universidad Diego Portales, ⁶Pontificia Universidad Católica de Chile, Programa de Neurociencias, ⁷Instituto de Neurociencias e Investigación.

PREVENTING SOCIAL ISOLATION SHOULDN'T WAIT FOR LATE ADULthood: IN *DROSOPHILA MELANOGASTER*, EARLY SOCIALIZATION PROTECTS BEHAVIOR AGAINST ISOLATION LATER IN LIFE.

INTRODUCTION

Social isolation is a well-documented modifiable risk factor for dementia, linked to cognitive decline and reduced cognitive reserve (Huang, 2023; Drinkwater et al., 2022). Yet social history may shape this vulnerability much earlier in life. Using *Drosophila melanogaster* given its functional homology with human stress-related neurotransmitters (Sokolowski, 2010) we tested whether early socialization protects behavioral stability against later isolation, explicitly accounting for sex given that effective interventions cannot ignore sex-specific vulnerability.

In 106 subjects, we compared three social histories: chronic isolation (Group A), early socialization followed by isolation (Group B), and continuous socialization (Group C).

METHODS

Subjects: *Drosophila melanogaster* (Canton-S), 106 individuals, both sexes, recorded at 1 and 4 weeks of adulthood. Three social histories:

- Group A chronic isolation
- Group B early socialization, then isolated
- Group C continuous socialization

Behavioral measures: 10-min video in a standardized grid: crossings, direction changes, jumps, resting episodes.

Statistics: Three-way ANOVA (Group × Age × Sex, Type III SS), with Welch's ANOVA and Games-Howell post-hoc for variance heterogeneity. Negative binomial GLM for jumps (overdispersed). R v4.6.0.

RESULTS

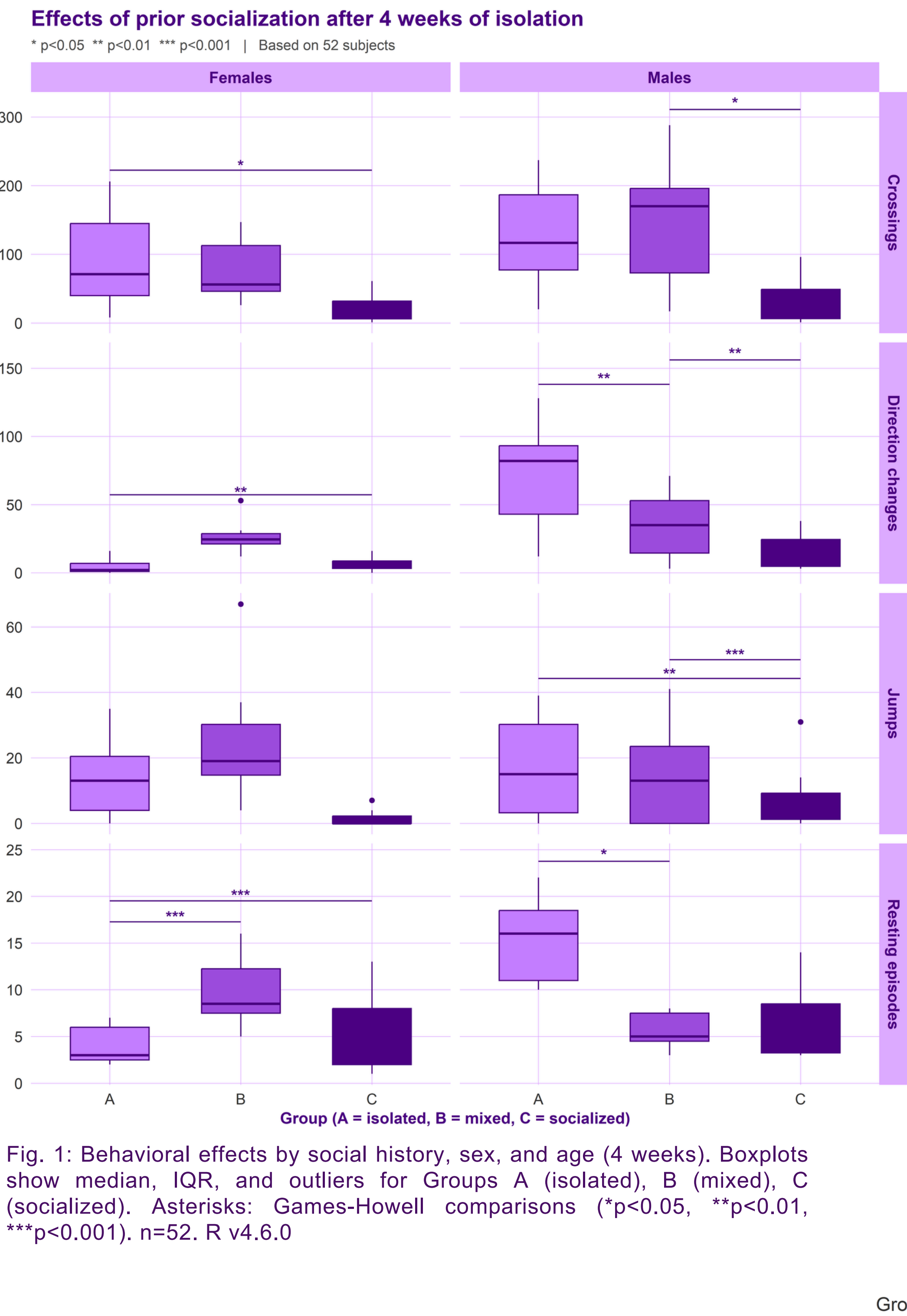


Fig. 1: Behavioral effects by social history, sex, and age (4 weeks). Boxplots show median, IQR, and outliers for Groups A (isolated), B (mixed), C (socialized). Asterisks: Games-Howell comparisons (*p<0.05, **p<0.01, ***p<0.001). n=52. R v4.6.0

Effect size (Fig. 2): largest for Age in resting episodes, followed by Group×Age×Sex interactions in resting episodes and direction changes—confirming that age and sex jointly shape isolation's behavioral impact.

Four locomotor variables were assessed across both sexes and three social histories.

Crossings (Fig. 1): significant Group and Age effects, emerging only at 4 weeks—males: B>C; females: A>C.

Direction changes (Fig. 1): a highly significant Group×Age×Sex interaction. At 4 weeks, males: A>B and A>C; females: B>A.

Jumps (Fig. 1): given overdispersion, a negative binomial model confirmed a Group effect. At 4 weeks in males, A>C (rate ratio=9.9) and B>C (rate ratio=17.8).

Resting episodes (Fig. 1): the study's strongest three-way interaction, reversed by sex at 4 weeks—males: A>B; females: B>A and C>A.

Effect size (partial eta squared) by behavioral variable

Three-way ANOVA, Type III sum of squares

	Crossings	Direction changes	Jumps	Resting episodes
Group	0.14	0.24	0.14	0.11
Age	0.06	0.00	0.00	0.36
Sex	0.01	0.10	0.03	0.05
Group x Age	0.02	0.03	0.03	0.08
Group x Sex	0.02	0.09	0.04	0.16
Age x Sex	0.03	0.16	0.05	0.09
Group x Age x Sex	0.00	0.18	0.00	0.25

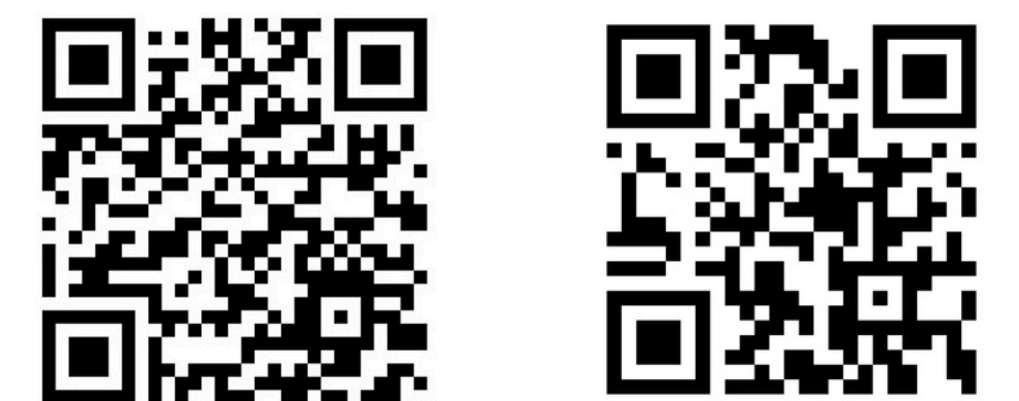
Fig. 2: Partial eta-squared (η^2_p) effect sizes, three-way ANOVA (Type III SS), complete dataset (n=106). R 4.6.0

DISCUSSION

These findings support the hypothesis that prior socialization modulates isolation's behavioral effects, depending on timing and sex (Yadav et al., 2024). Effects emerged only at 4 weeks, suggesting accumulation with sustained isolation paralleling cognitive decline in isolated older adults. The sex-reversed resting pattern further suggests a dimorphic vulnerability often overlooked in dementia research (Vora et al., 2022).

Dementia prevention should not be limited to late adulthood: early socialization may also protect long-term behavioral trajectories. This study is limited by group imbalance and the absence of neurochemical data, which planned HPLC quantification will address.

CONTACT REFERENCES



millaray.pizarro@ug.uchile.cl
fdelpino@med.uchile.cl
christinegierke@uchile.cl