EFFECTS OF DEVELOPMENTAL EXPOSURE TO BISPHENOL A ON BEHAVIOR AND GUT MICROBIOME OF CALIFORNIA MICE (*PEROMYSCUS CALIFORNICUS*) IN THE F1 GENERATION

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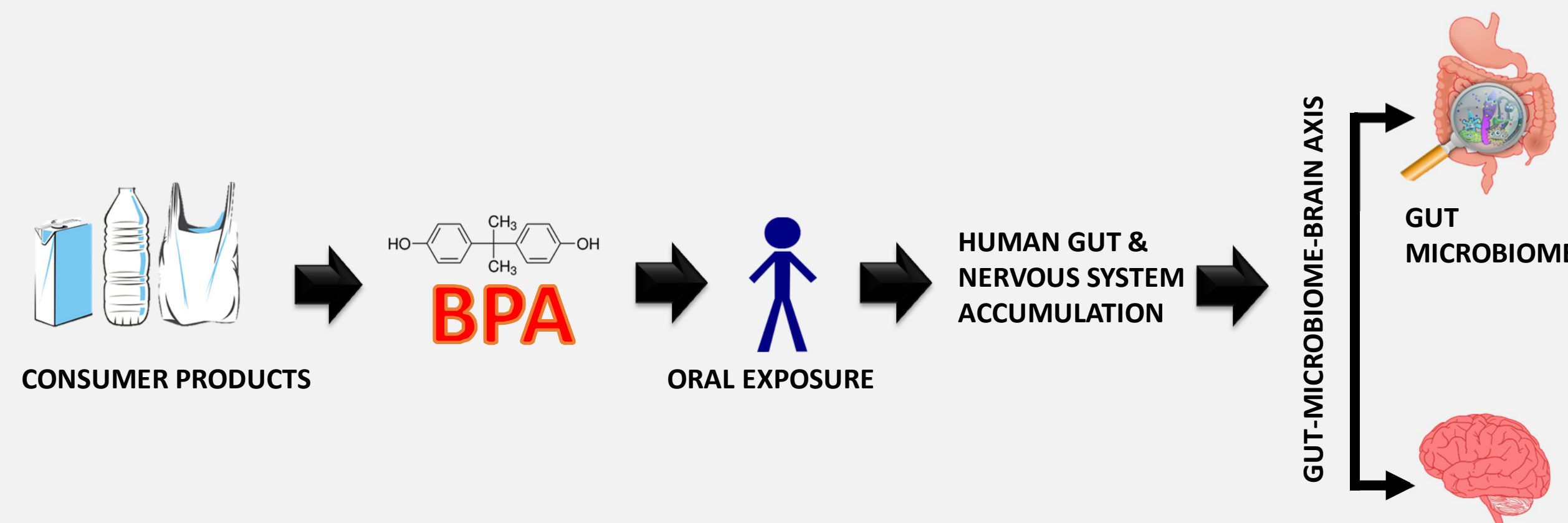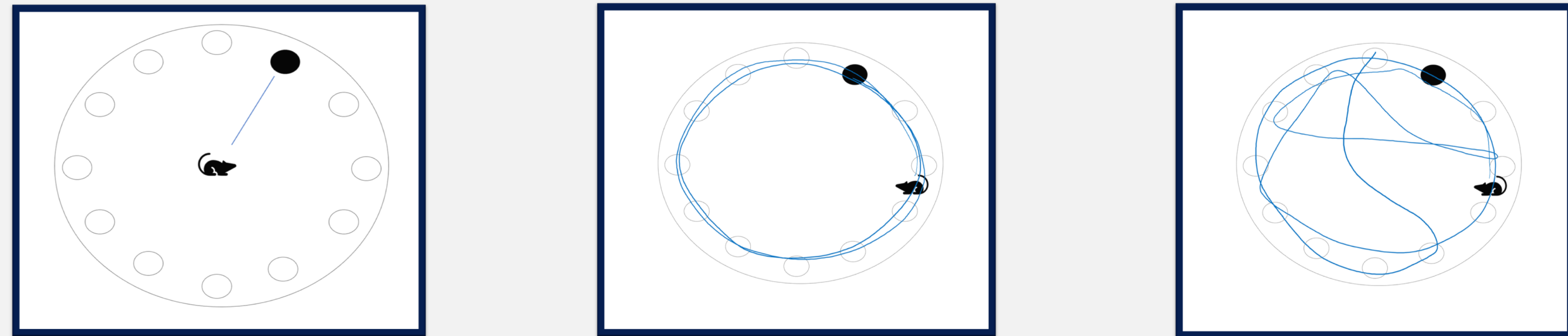
BACKGROUND

- Bisphenol A (BPA) is an industrial chemical used to produce many commonly used household items.
- Developmental exposure to BPA may affect the gut microbiome and this may contribute to neurobehavioral disorders affecting behavioral domains disrupted in ASD children.
- In utero exposure to environmental chemicals may increase the risk of neurobehavioral disorders.

AIM AND HYPOTHESIS

- California mice developmentally exposed to BPA will demonstrate impairments in social, communication, learning, and memory behaviors. This group of animals are also predicted to demonstrate increased anxiety-like behaviors. Both males and females will be tested to examine for potential sex differences.
- We hypothesize that BPA causes gut microbiome dysbiosis leading to increased risk of neurobehavioral disorders.

EXPERIMENTAL DESIGN

- To examine the effects of BPA, P0 female California mice were exposed to BPA (50mg/kg per feed weight) two weeks prior to breeding (periconception period) throughout gestation and lactation as postnatal brain development is comparable to the third trimester in the human.

Behavioral analysis

- Behavioral tests that are currently being performed include, Barnes maze (Fig. 1) to test spatial learning and memory, and reverse Barnes in which the inverse hole was used to examine for deficits in cognitive plasticity. Animals are being tested in the Elevated Plus Maze (EPM) to measure anxiety-like and exploratory behaviors. (Fig. 4)
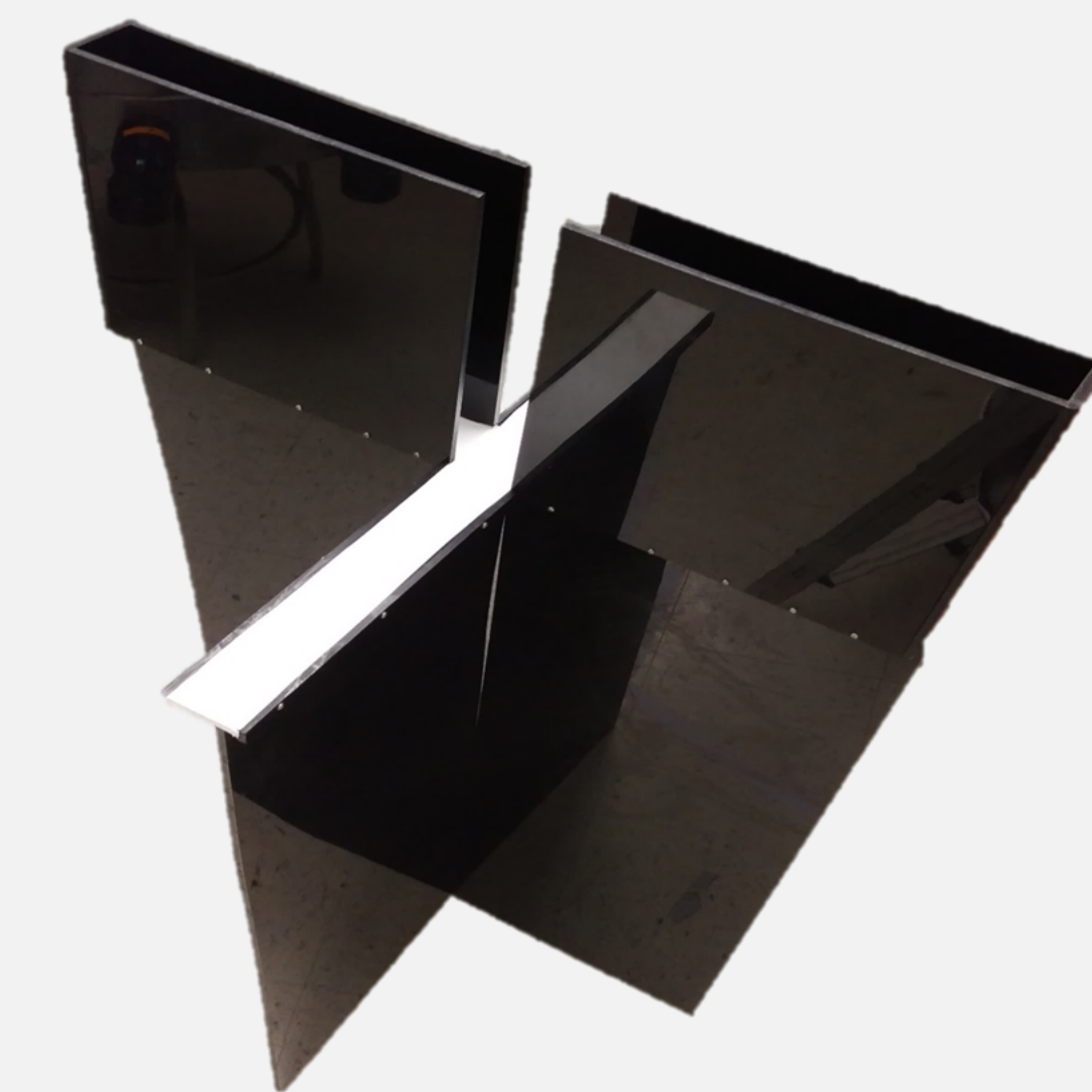
Social interactions

- Social interactions are being evaluated by recordings of mice exposed to one or two stranger mice (Fig. 3), and communication assessed by analyzing their audible and ultrasonic vocalizations. (Figure 2A, 2B)

Fecal microbiome

- Fecal microbiome will be examined by using PowerFecal® DNA isolation kit at various ages in the same F1 individuals that will undergo behavioral testing to determine whether gut microbiome changes are associated with behavioral deficits.
- The 16S rRNA sequencing approach will be used to assess this microbiome.

Barnes maze and Reverse Barnes Maze

Fig 1. Schematic diagram of the Barnes Maze illustrating different navigational strategies used to locate correct exit hole: direct (left), serial (middle) and random (right).
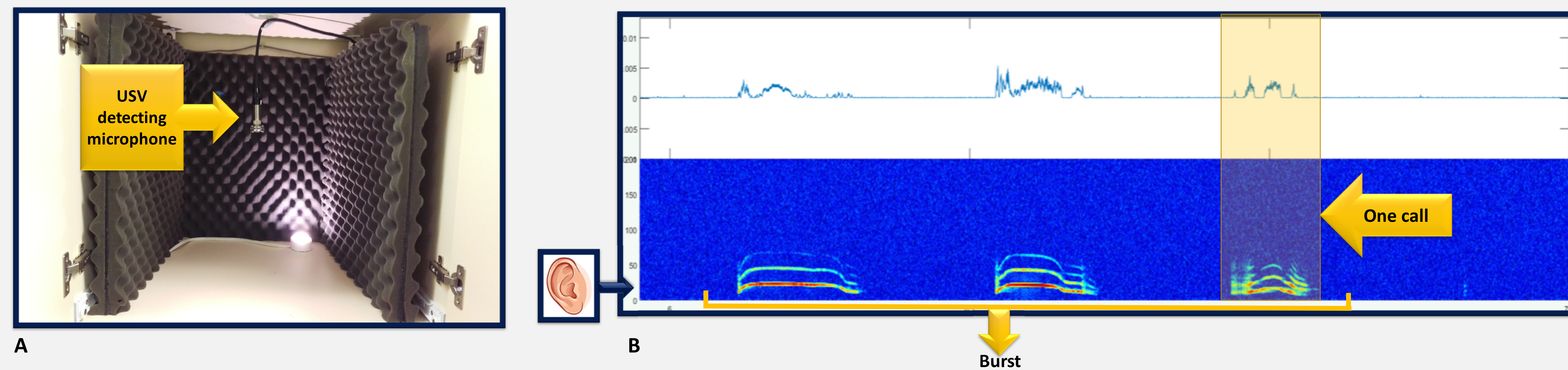
Fig 2. A) The setup includes a box lined with sound-proof foam, an overhead Avisoft Bioacoustics Ultrasonic Microphone. Their vocalizations were recorded for 3-5 minutes. B) Example recordings for audible and USV sounds produced by California mice pups. A burst is defined as a group of calls that are separated from another burst by an interval in time that is statistically longer the mean time between calls. At approximately 20kHz is the maximum range of hearing for humans, above this mark is established as ultrasonic.

Fig 3. Social interaction and affiliation is evaluated by using the three chamber test.

Fig 4. Elevated Plus Maze used to assess anxiety-like behavior by evaluation of number of entries into the closed arms.

CONCLUSION AND FUTURE AIM

- The studies are currently ongoing but the animals appear to be handling the behavioral tests well.
- We have been able to obtain meaningful data.
- Continue behavioral tests
- Perform gut microbiome assessments.

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