

Age-related attention sensitivity is different in monogenic etiologies relative to idiopathic autism



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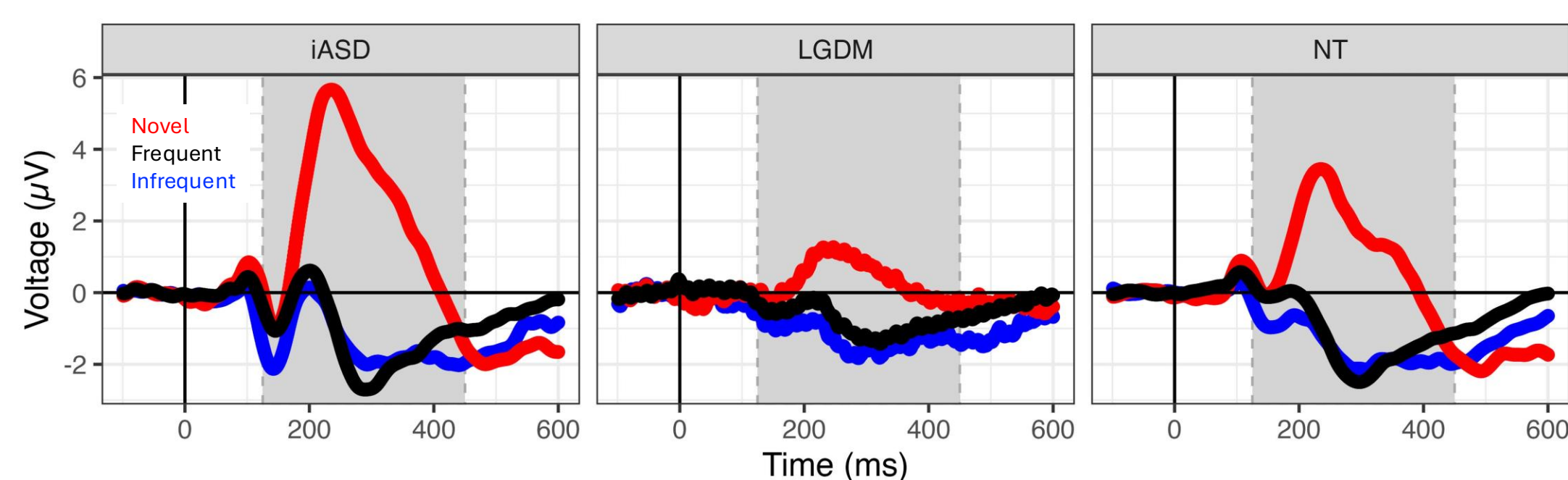
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BACKGROUND

Attention is a foundational basis for social communication impairments in autism, yet the natural time course of how attention supports social communication across genetic and biological levels remains unclear. Biological measures of attention may serve as clinical guides for diagnosis, monitoring, or prognostication, such as the P3 component via electroencephalography (EEG). It is increasingly important to consider and anticipate age-related changes. Working with monogenic subgroups with a known likely gene-disrupting mutation (LGDM) provides an opportunity to build from common biological foundation/s compared to idiopathic autism (iASD) without a known genetic etiology.

METHODS

| | Likely-gene disrupting mutation | Idiopathic ASD | Neurotypical |
|------------|---------------------------------|----------------|--------------|
| N | 198 LGDM | 62 iASD | 73 NT |
| Age M(SD) | 9.95 (6.31) | 12.4 (2.5) | 10.8 (4.11) |
| Range | 6 m – 38 years | 7-18 years | 4-18 years |
| NVIQ M(SD) | 60.2 (30) | 90.8 (25.5) | 116.0 (15.3) |
| ASD Dx | 61.1% | 100% | 0% |
| ID Dx | 76.3% | 24.5% | 0% |



Auditory attention oddball task during EEG recording (Hudac et al., 2018). Primary outcome = P3 amplitude

Age-related attention is different for monogenic relative to idiopathic autism.

- Genetic subgroups exhibited moderate attention effects that were predicted to increase across age, yet these effects decrease over age for iASD.
- Dynamic responses to novelty (i.e., patterns of change within the experiment), did not vary by age for the LGDM group.

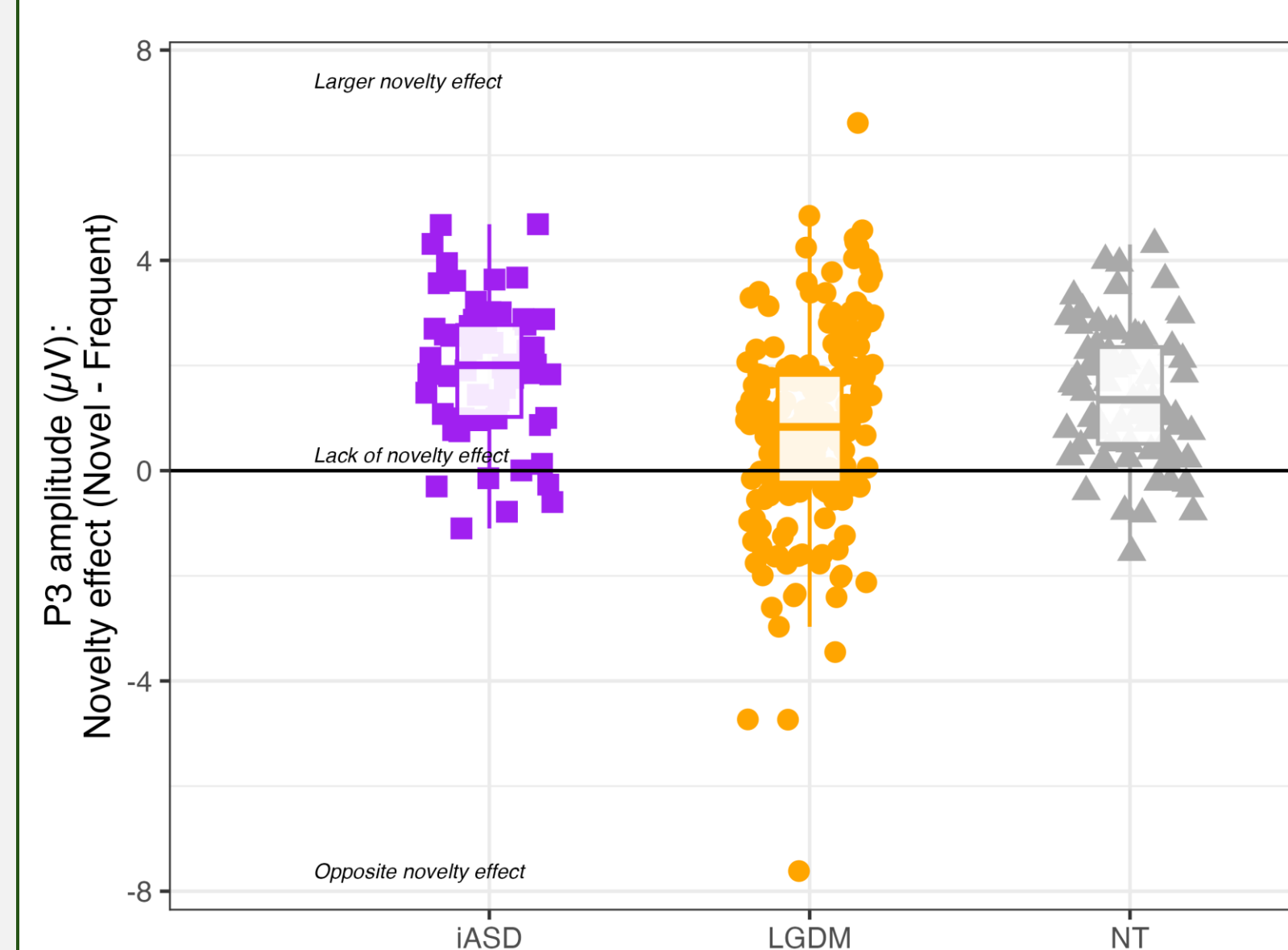
“Learning style” may be a potential biomarker of learning for genetic subgroups as a potential clinical trial endpoint.

OBJECTIVES

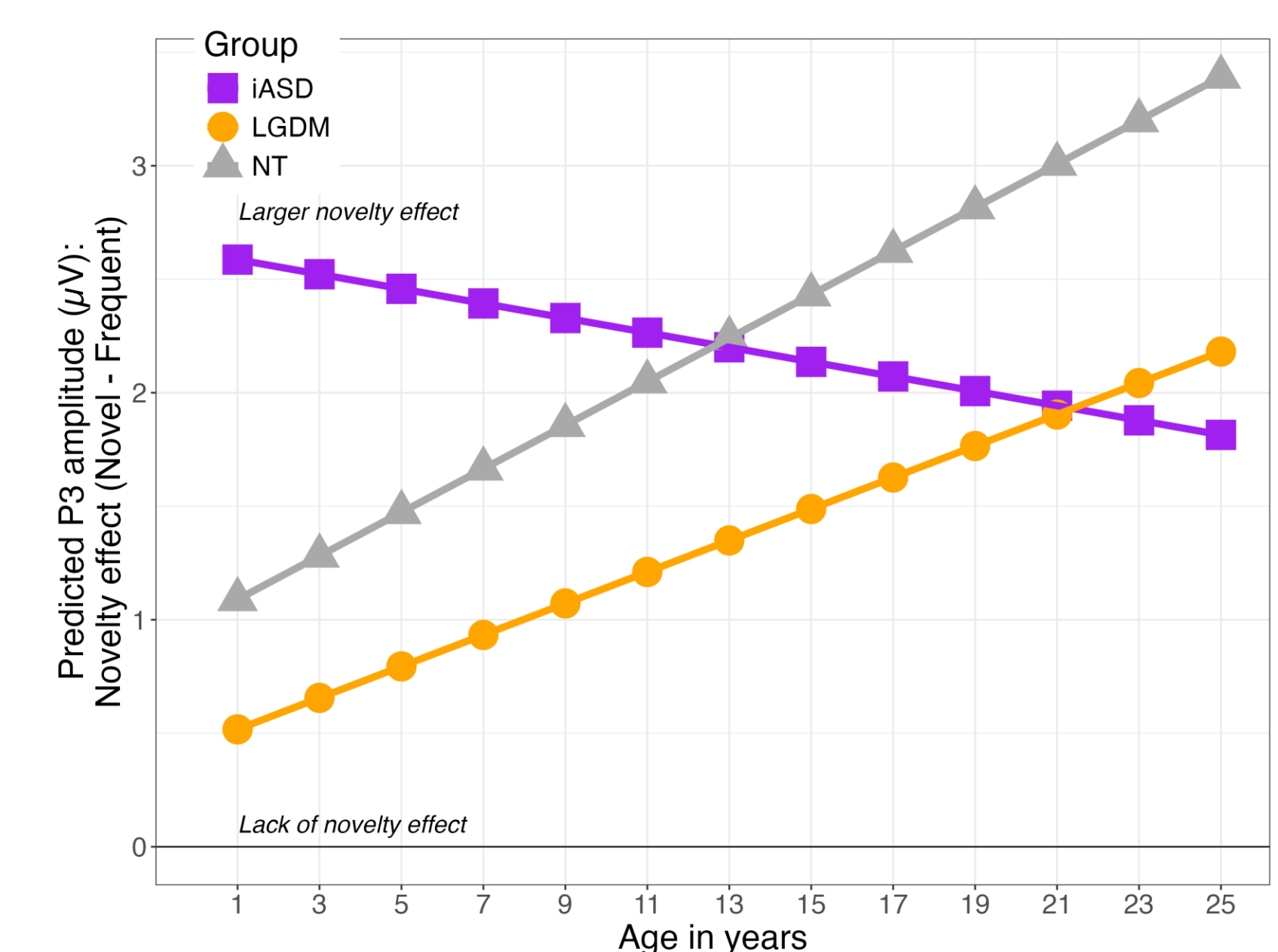
- Assess whether there are age-related changes in a candidate biomarker of attention (P3 novelty response)
- Evaluate whether and how attention responses may dynamically shift within a single experimental session, as a metric of learning style.

RESULTS

1A. Larger novelty effects in iASD than LGDM or NT



1B. Decreasing effects over age for iASD but increasing over age for LGDM and NT



1C. Variability in attention effect across monogenic LGDM subgroups

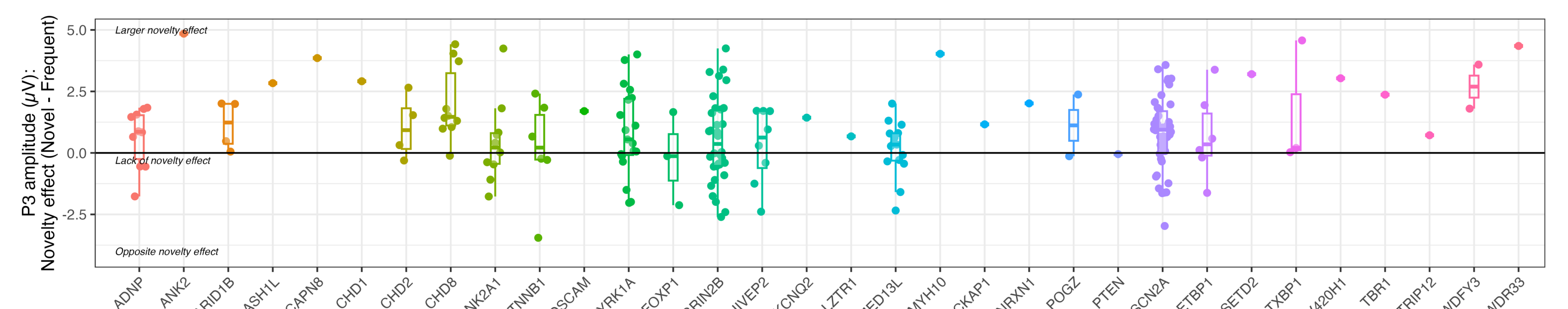


Figure 1. Individual differences in novelty effects (Panel A) and predicted age-related changes (Panel B). More positive values indicate a larger novelty effect. Panel A: Condition effects are plotted for each person as points with barplots summarizing at the group level. Panel B: Model-predicted age effects indicate decreasing effects across age for iASD (slope = -.032), increasing effects for LGDM (slope = .068) and NT (slope = .086). Panel C: Effects for each gene subgroup.

2. Novelty habituation varies as a function of age in iASD and NT but not for LGDM

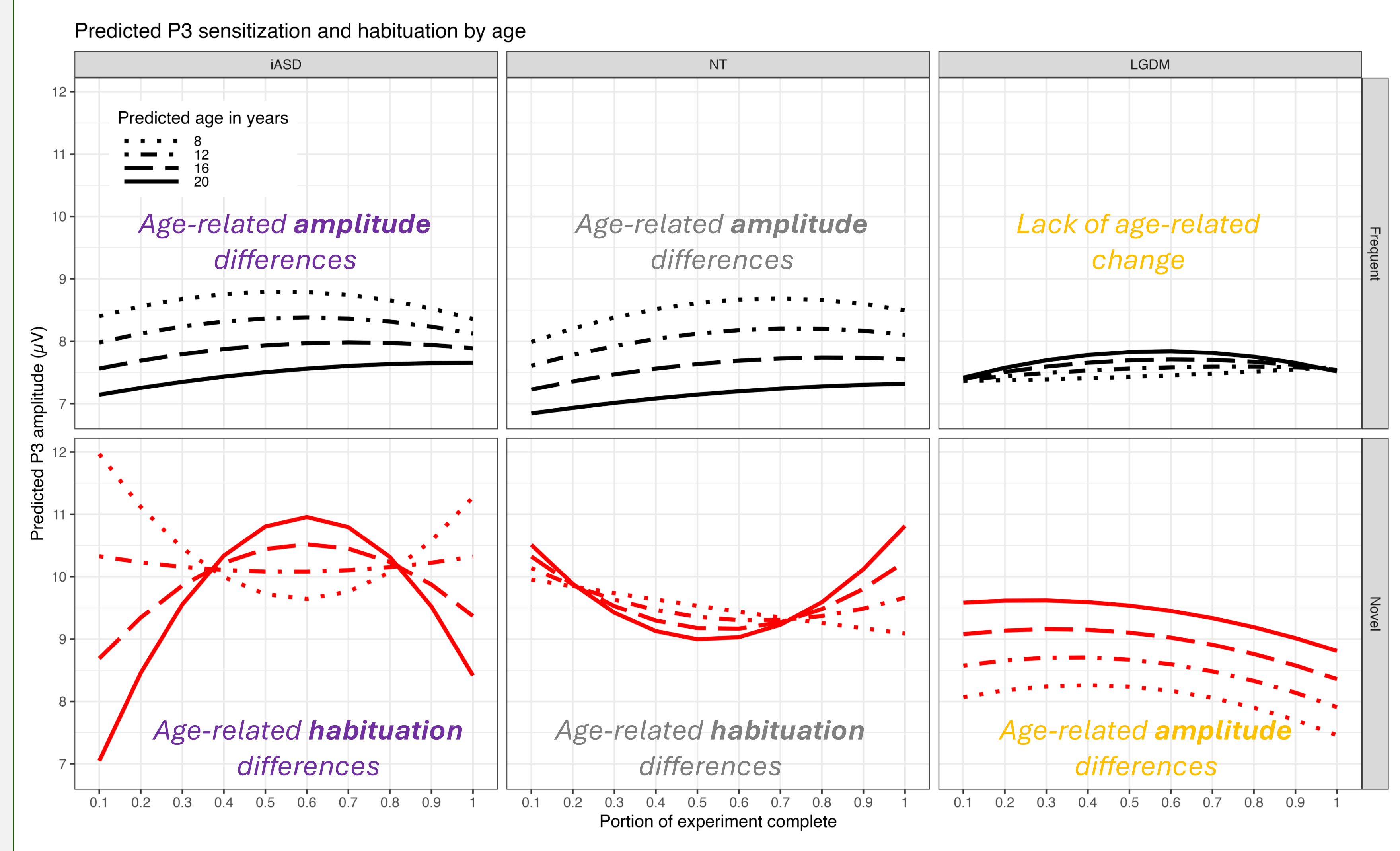


Figure 2. Patterns of habituation (i.e., decreasing over time) and sensitization (i.e., increasing over time) of the P3 amplitude for each group. Model-predicted P3 amplitude indicated (1) lack of age-related difference to frequent tones in LGDM but age-related amplitude shifts in iASD and NT, (2) similar weak novel habituation across age in LGDM, (3) similar early and rapid novel habituation in NT, and (4) age-related dynamic differences in iASD, as described above.



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