


Defining Clusters of Young Autistic and Typically-Developing Children Based on Loudness-Dependent Auditory Electrophysiological Responses

CURRENT STATUS: UNDER REVISION

 Molecular Autism  BMC

Patrick Dwyer
University of California Davis

 patricksrdwyer@gmail.com *Corresponding Author*
ORCID: <https://orcid.org/0000-0003-1779-5252>

Xiaodong Wang
University of California Davis

Rosanna De Meo-Monteil
University of California Davis

Fushing Hsieh
University of California Davis

Clifford D. Saron
University of California Davis

Susan M. Rivera
University of California Davis

DOI:

10.21203/rs.2.22455/v1

SUBJECT AREAS

Cellular & Molecular Neuroscience

KEYWORDS

Autism, heterogeneity, hierarchical clustering, event-related potentials (ERPs), subgroups, sensory processing

Abstract

Background: Autistic individuals exhibit atypical patterns of sensory processing that are known to be related to quality of life, but which are also highly heterogeneous. Previous investigations of this heterogeneity have ordinarily used questionnaires and have rarely investigated sensory processing in Typical Development (TD) alongside Autism Spectrum Development (ASD). **Methods:** The present study used hierarchical clustering in a large sample to identify subgroups of young autistic and typically-developing children based the normalized global field power (GFP) of their event-related potentials (ERPs) to auditory stimuli of four different loudness intensities (50, 60, 70, 80 dB SPL): that is, based on an index of the relative strengths of their neural responses across these loudness conditions. **Results:** Four clusters of participants were defined. Normalized GFP responses to sounds of different intensities differed strongly across clusters. There was considerable overlap in cluster assignments of autistic and typically-developing participants, but autistic participants were more likely to display a pattern of relatively linear increases in response strength accompanied by a disproportionately strong response to 70 dB stimuli. Autistic participants displaying this pattern trended towards obtaining higher scores on assessments of cognitive abilities. There was also a trend for typically-developing participants to disproportionately fall into a cluster characterized by disproportionately/nonlinearly strong 60 dB responses. Greater auditory distractibility was reported among autistic participants in a cluster characterized by disproportionately strong responses to the loudest (80 dB) sounds, and furthermore, relatively strong responses to loud sounds were correlated with both auditory distractibility and noise distress. This appears to provide evidence of coinciding behavioural and neural sensory atypicalities. **Limitations :** Replication may be needed to verify exploratory results. This analysis may ignore some variability related to classical ERP latencies and topographies. The sensory questionnaire employed was not specifically designed for use in autism. Variability in sensory responses unrelated to loudness is ignored, leaving much room for additional research. **Conclusions:** Taken together, these data demonstrate the broader benefits of using electrophysiology to explore individual differences. They illuminate different neural response patterns and suggest relationships between sensory neural responses and sensory behaviours, cognitive

abilities, and autism diagnostic status.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed.

However, the manuscript can be downloaded and accessed as a PDF.

Figures

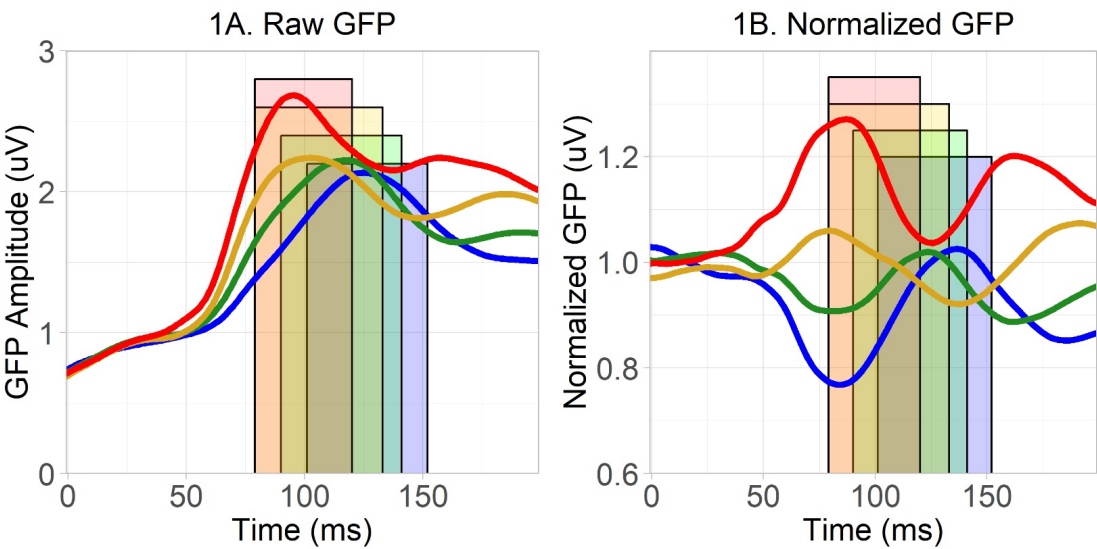


Figure 1

1A. Raw GFP from 0 to 200ms post-stimulus onset averaged, separately in each loudness condition, across all participants in both diagnostic groups. The overlapping coloured rectangles represent the different 85% fractional peak latency time windows from each of the loudness conditions. Figure 1B. Normalized GFP averaged across all participants in each loudness condition.

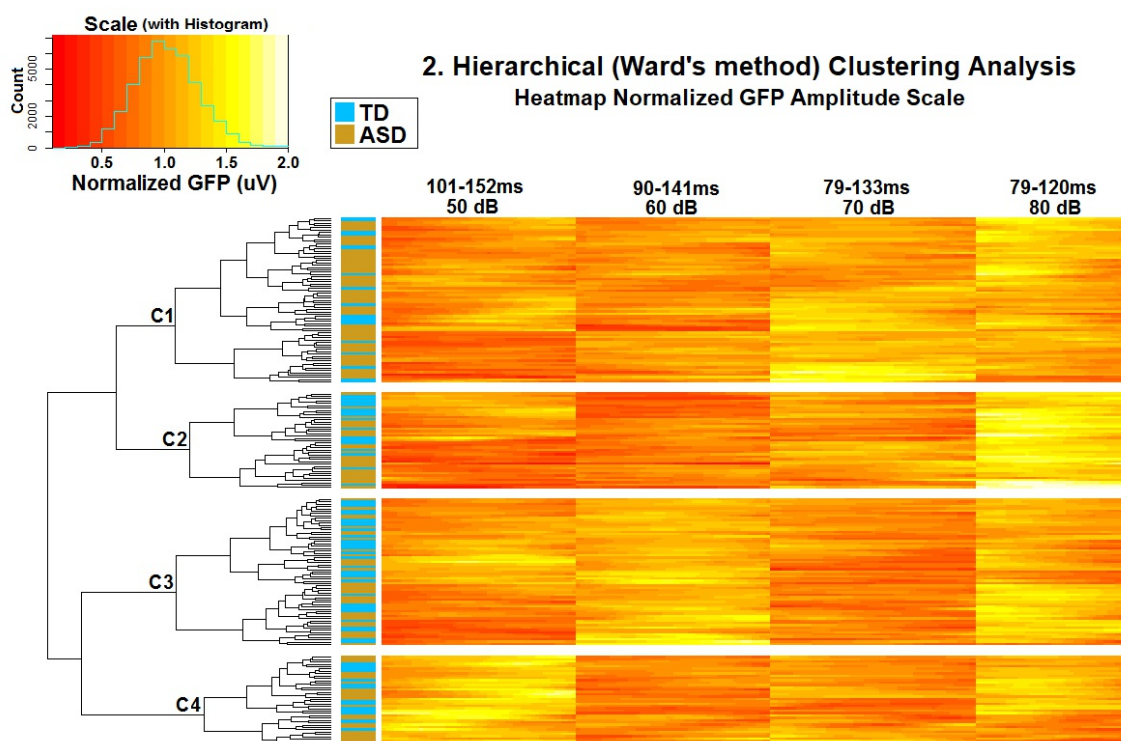


Figure 2

The hierarchical clustering analysis using Ward's method. Each row is a participant, with autistic participants being marked as gold in the small column on the left, while typically-developing participants are blue. The four main columns show normalized GFP in each loudness condition. Each column also depicts changes in normalized GFP over time, with

earlier time-points being on the left of each column and later time-points on the right of each column. As shown in the scale in the upper left corner, smaller (reflecting a weaker normalized GFP in the loudness condition) are redder, while larger values (reflecting a stronger GFP) are yellower. A histogram showing the distribution of individual data points (individual data points represent a participant's normalized GFP value in a given condition and at a given time-point) is superimposed over the scale. The dendrogram on the far left shows hierarchical clusters of similar participants. The horizontal lengths of the dendrogram branches represent the distance between clusters. The clusters selected for the purposes of this analysis are separated by blank space, and group numbering proceeds from top to bottom (i.e., C1 is at the top, C4 is at the bottom).

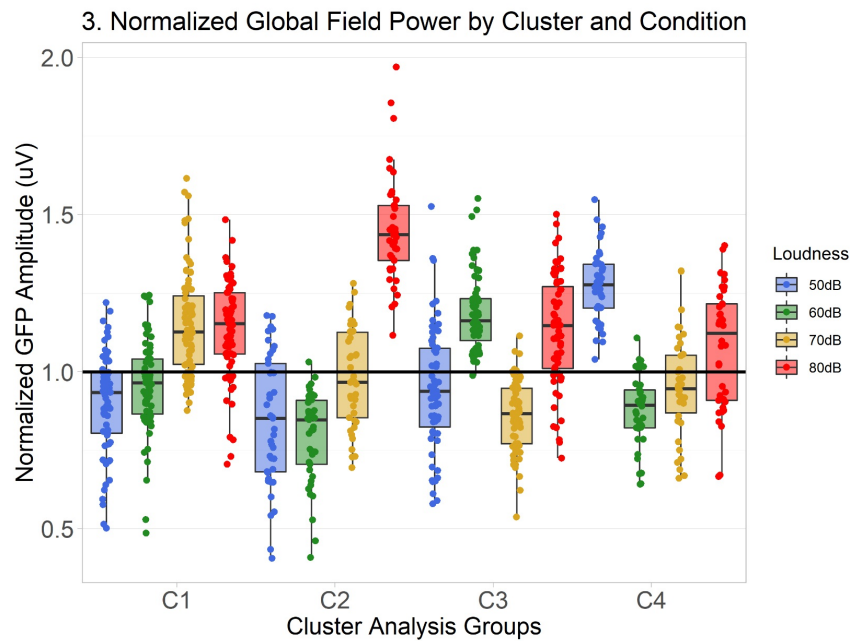
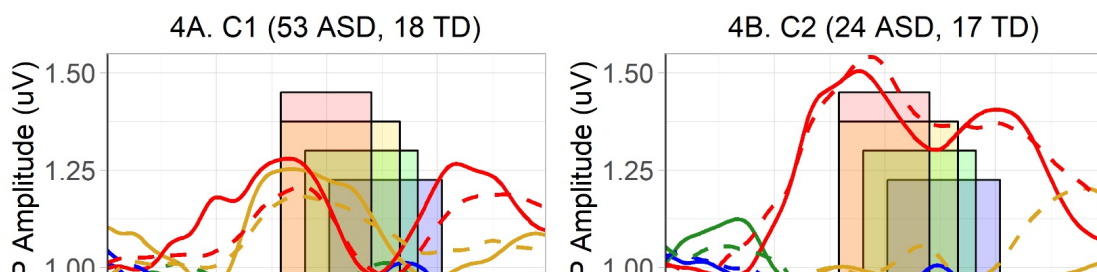


Figure 3

Normalized GFP averaged across clustering time windows in each loudness condition and cluster collapsed across both diagnostic groups. C1 contains 53 autistic and 18 typically-developing participants, C2 contains 24 autistic and 17 typically-developing participants, C3 contains 32 autistic and 31 typically-developing participants, and C4 contains 23 autistic and 15 typically-developing participants. Hinges (outer limits of boxes) correspond to first and third quartiles (25th and 75th percentiles) and whiskers extend either 1.5x the interquartile range outwards from the boxes, or the range of the data, whichever is smaller.



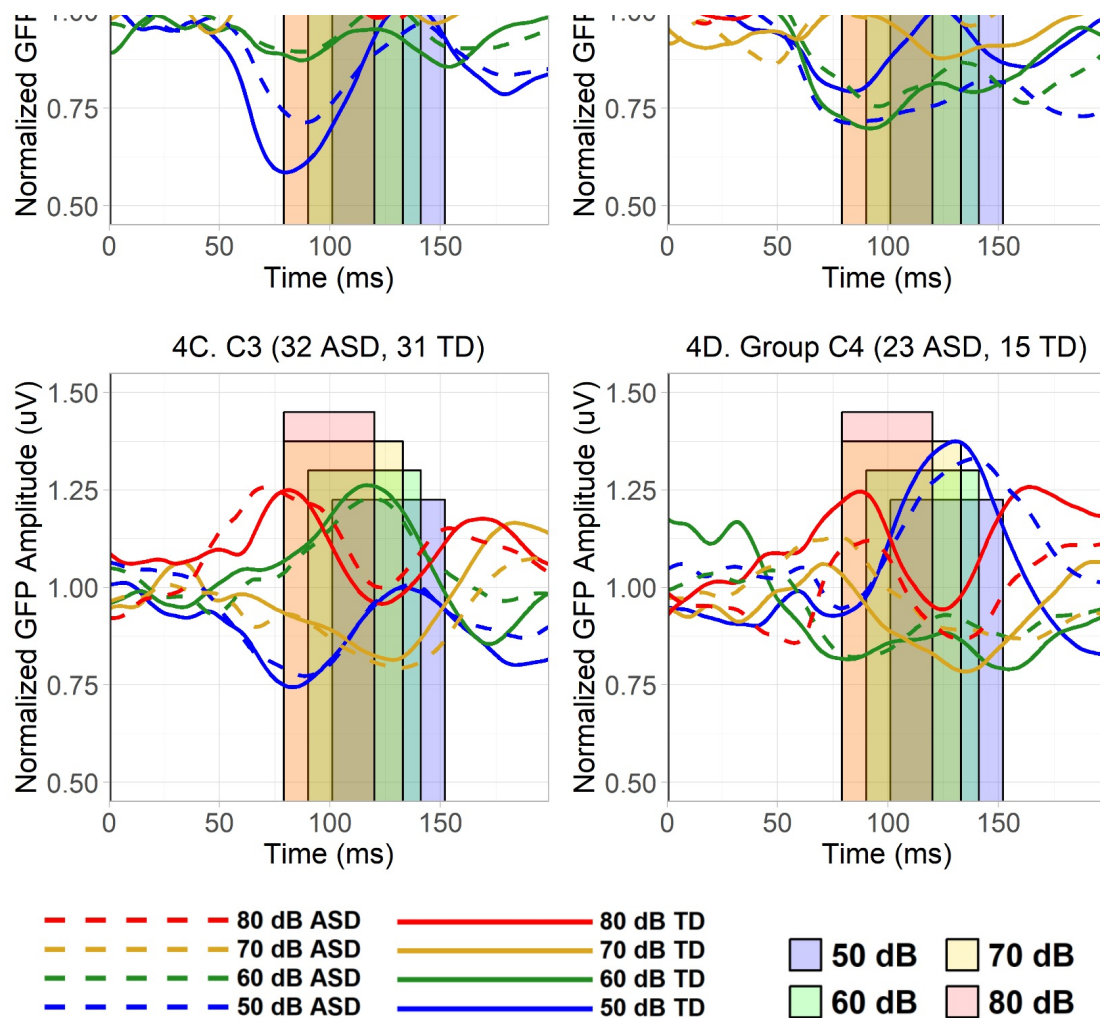


Figure 4

A. Normalized GFP averaged, separately in each loudness condition and diagnostic group, across participants from C1. The overlapping coloured rectangles represent the different 85% fractional peak latency time windows from each of the different loudness conditions. B. Normalized GFP averaged across participants in each diagnostic group from C2. C. Normalized GFP averaged across participants in each diagnostic group from C3. D. Normalized GFP averaged across participants in each diagnostic group from C4.

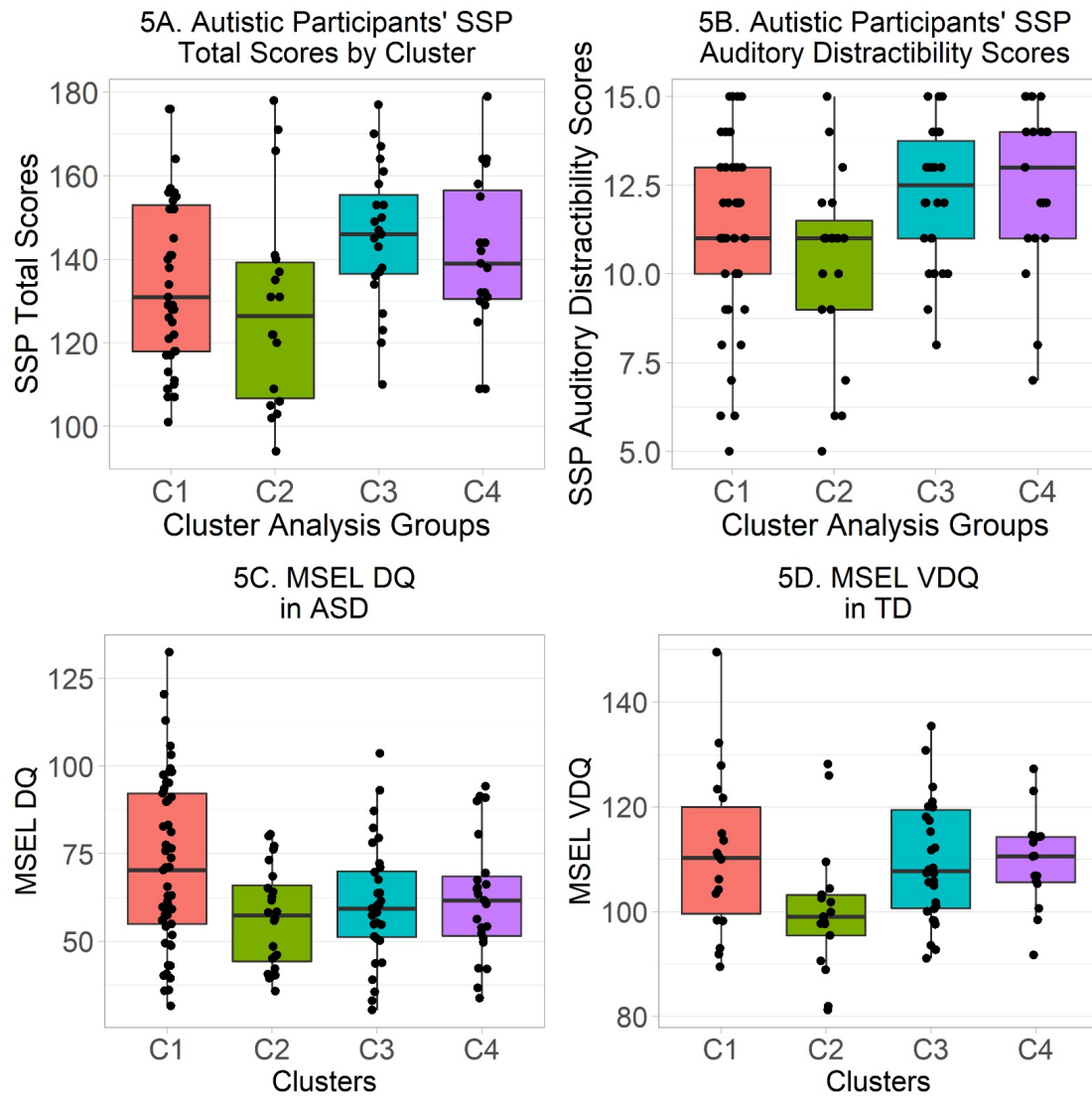


Figure 5

A. Total SSP scores in autistic participants from each cluster. Counting only those with complete SSP data, C1 contains 39 autistic participants, C2 contains 18 autistic participants,

C3 contains 23 autistic participants, and C4 contains 19 autistic participants. Outer limits (hinges) of boxes correspond to first and third quartiles (25th and 75th percentiles) and whiskers extend either 1.5x the interquartile range outwards from the boxes, or the range of the data, whichever is smaller. B. SSP Auditory Distractibility scores in autistic participants from each cluster. Counting only those with complete SSP Auditory Distractibility data, C1 contains 41 autistic participants, C2 contains 19 autistic participants, C3 contains 26 autistic participants, and C4 contains 19 autistic participants. C. MSEL DQ in autistic participants from each cluster. D. MSEL VDQ in typically-developing participants from each cluster.

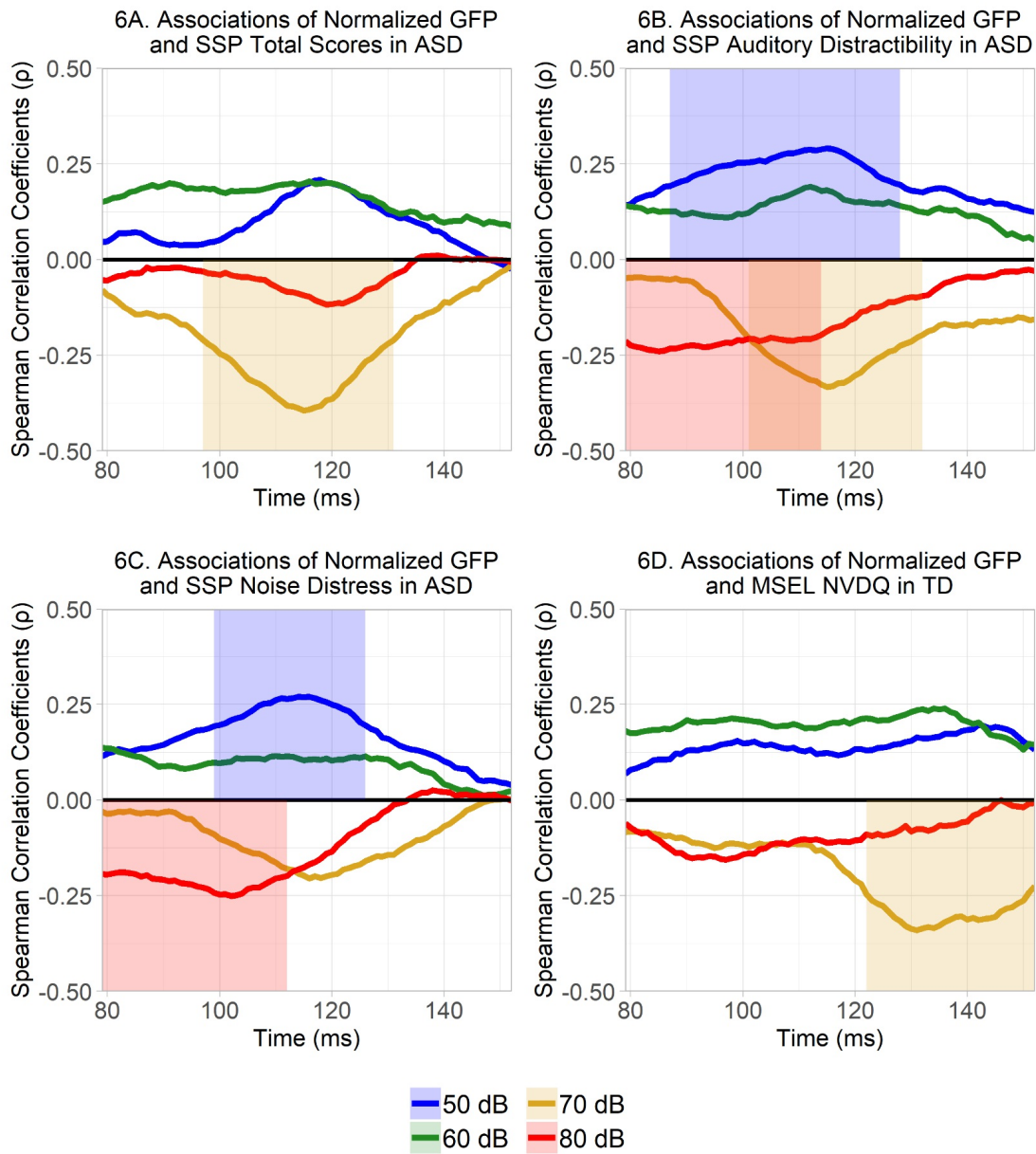


Figure 6

Spearman's correlation coefficients between normalized GFP in each condition, separately at each consecutive time-point, and other measured variables. Time windows with positive

correlation effects in any loudness condition are highlighted above the zero-line, while time windows with negative correlation effects in any loudness condition are highlighted below the zero-line. Values at any given time point represent the Spearman's correlation coefficient value at that time point. A. Spearman's correlation between normalized GFP and SSP total scores in ASD. B. Spearman's correlation between normalized GFP and SSP auditory distractibility in ASD. C. Spearman's correlation between normalized GFP and SSP noise distress in ASD. D. Spearman's correlation between normalized GFP and MSEL NVDQ in TD.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

[2020_01_29 supporting info.pdf](#)