10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

EU-AIMS Autism Research in Europe

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Exploring electrophysiological markers of auditory processing in Autism Spectrum Disorder during the odd-ball task: evidence from the EU-AIMS LEAP cohort.

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Facts & Figures

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Contributions	
IMI funding:	20 490 981 €
EFPIA in kind:	9 773 543 €
Other:	7 216 089 €
Total Cost	37 480 613 €
Project website:	www.eu-aims.eu
Social media:	Twitter @euaims

The LEAP (Longitudinal European Autism Project) is part of EU-AIMS. It is the largest multi-centre, multi-disciplinary observational study in the world to date, aiming to identify and validate stratification biomarkers for ASD. This poster presents the MMN EEG data from LEAP.

Challenge

One core symptom domain of ASD is 'repetitive behaviours', under which falls sensory processing abnormalities. One potential explanation for these abnormalities has been *reduced* habituation/attenuation of sensory information. This process can be indexed by the mismatch negativity (MMN) EEG component. As hypothesised in the predictive coding account of ASD (Lawson, Rees & Friston, 2014), reduced habituation should be associated with a smaller MMN. Yet, previous findings are mixed, likely due to small sample sizes and the heterogeneous nature of ASD (see Uljarević et al, 2011). The MMN has been termed a candidate endophenotype for autism (Gomot, 2011)

Aims: 1) To conduct a systematic review of the literature, to identify the range of sample sizes used, the effect size, and to test for publication bias. 2) To test these effects empirically in a large heterogeneous cohort of individuals with ASD (LEAP sample).

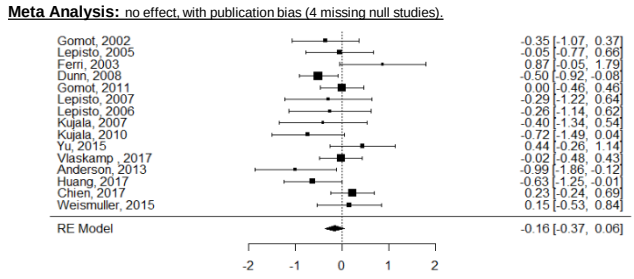
Approach & Methodology

Meta-analysis: 1327 studies were identified and reviewed. 15 studies were classified as relevant (auditory oddball task, with case-control design). EU-AIMS LEAP analysis: A total of 1400 trials of four different stimuli were used in the auditory mismatch negativity task: Standard (1066); Frequency deviants (78); Duration Deviants (78); Combined frequency & duration deviant (78). Eye blinks and saccades were removed with ICA. A -100 to +100 threshold was used to remove artefacts. The baseline period was -100 to 0ms.

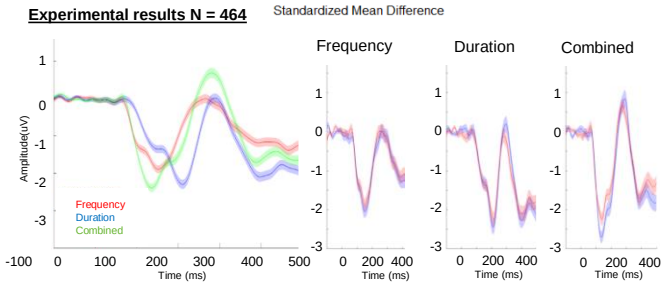
Participant Schedule	Diagnostic group	N	Total N
Children	ASD	60	106
	TD	46	
Adolescents	ASD	78	147
	TD	69	
Adults	ASD	77	142
	TD	65	
Adol. & adults (IQ <75)	ID-ASD	48	69
	ID-control	21	

Results

Meta Analysis: no effect, with publication bias (4 missing null studies).



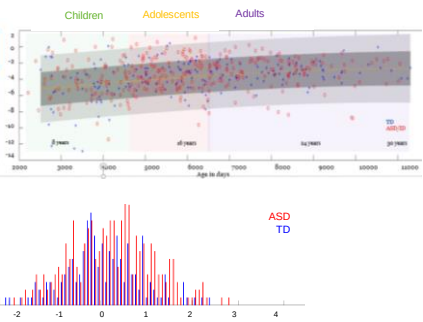
Experimental results N = 464



The duration MMN occurred significantly later than the frequency and combined MMN (F=.118.48, p<.00001). No significant case-control differences in amplitude or latency (p>.05)

Normative modelling

ASD participants	TD normative mean
3.82%	>2SD
17.36%	1-2SD
68.40%	Mean+/-1 SD
7.29%	-1-2SD
3.13%	<2SD



Value of IMI collaboration

We have collected and analysed the largest comprehensive MMN EEG dataset in ASD to evaluate MMN as a potential biomarker.

We demonstrated the quality of the dataset and pre-processing by within-condition experimental effects. We provide evidence against the utility of the MMN as a biomarker for ASD.

Impact & take home message

The Meta analysis suggests an absence of a case-control difference between the ASD and TD groups in terms of an auditory MMN at frontal central electrodes. Most prior studies had small sample sizes.

This was corroborated by analysis of the LEAP dataset (large sample size: 464) at Fz where neither the amplitude or latency of the MMN differed at a case-control level.

Normative modelling demonstrated that the large percentage of ASD/ID participants fell within 1SD of the TD mean. Data driven analysis is needed to examine topographic effects, as well as trial by trial patterns in the MMN response.

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