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Longitudinal relations between mismatch negativity and psychological difficulties in mid-adolescence

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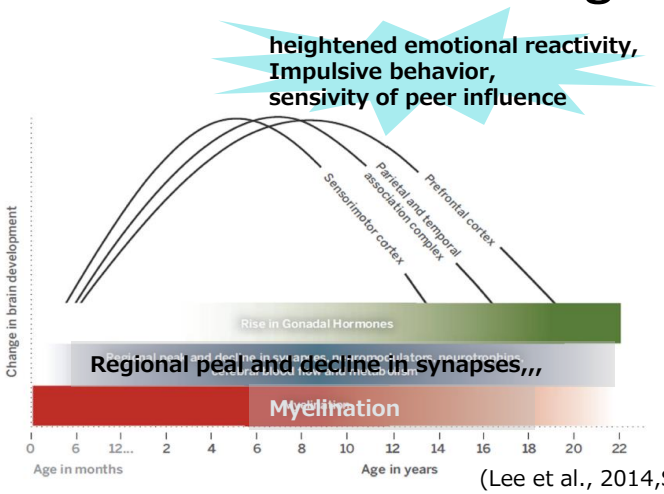
Outline

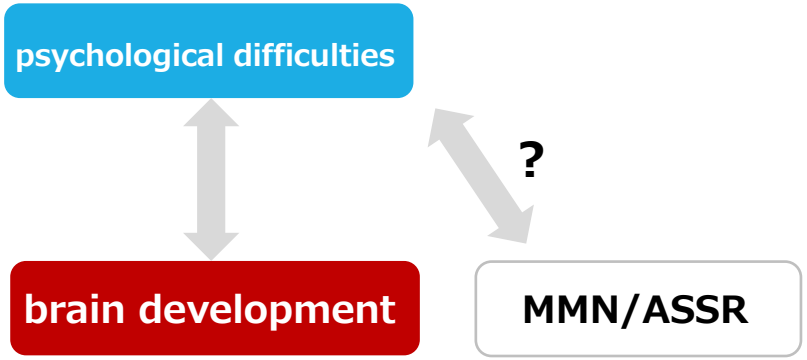
- This study investigated longitudinal associations between mismatch negativity (MMN), gamma-band auditory steady-state response (ASSR) and psychological difficulties in healthy mid-adolescents.
- As a result, decrease of MMN amplitude for duration changes were significantly associated with worse of psychological difficulties.
- Atypical development of MMN amplitude that reflects glutamatergic neurotransmission may affect psychological difficulties in mid-adolescence.

Introduction

- Adolescence is a crucial life stage for psychological difficulties



(Lee et al., 2014,Science)



- Mismatch negativity (MMN) / gamma-band auditory steady-state response (ASSR)

✓non-inverse electroencephalography (EEG) measures

✓develop during adolescence (e.g., Bishop et al., 2011 Cho et al., 2015)

✓each biomarkers reflect on glutamatergic and GABAergic neurotransmission (Tada et al., 2019, 2020) which is important on adolescent brain development

Our study aim

to investigate longitudinal associations between psychological difficulties and MMN, ASSR in healthy adolescents

Method

- Participant

【青春期の健康・発達調査】 TEEN COHORT

Large-longitudinal general population-based birth cohort targeting adolescence **(N=3171)**
Questionnaire, interview survey, cognitive task…

Population-neuroscience study of the Tokyo TEEN Cohort **(N=301)**

pn-TTC1 (N=301)
MRI, Questionnaire…
10 years old～

pn-TTC2
*Start **EEG measure (N=119)**, **Questionnaire**, MRI…*
12 years old～

pn-TTC3
***EEG measure (N=67)**, **Questionnaire**, MRI…*
14 years old～

pn-TTC4
Now measuring …
16 years old～

Time 1 **Time 2**

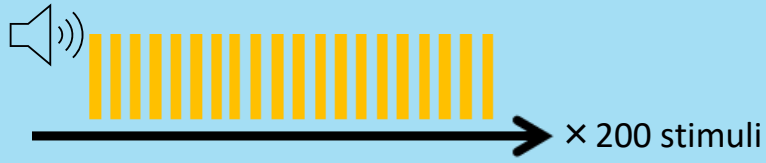
Method

- Psychological difficulties

Total difficulties score of the Strengths and Difficulties Questionnaire (SDQ-TD; Goodman, 1997) assessed by primary parent

- 4 EEG indices

Polymate, 2-channel (Fz, Cz)→ Analyzed channel: Fz
Reference: left mastoid

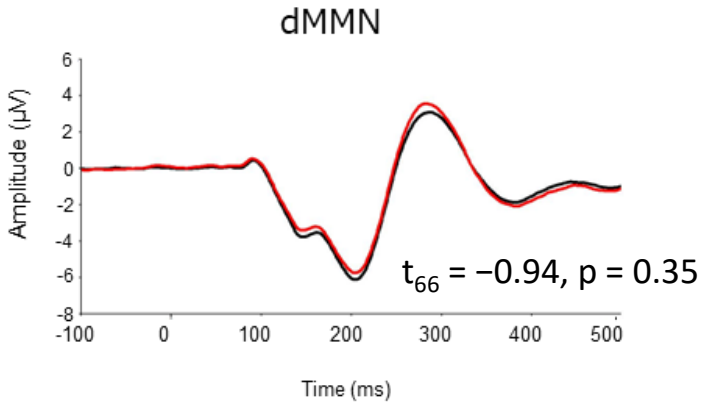
Indices	Task	Calculation
Duration MMN	Passive Oddball task Standard stimuli (90%, 1800) 1000Hz,50ms Deviant stimuli (10%, 200) 1000Hz, 100ms	Average amplitude around the peak of grand-average MMN wave (±25ms)
Frequency MMN	Passive Oddball task Standard stimuli (90%, 1800) 1000Hz,50ms Deviant stimuli (10%, 200) 1200Hz, 50ms	
Event-related spectral perturbation (ERSP) of **ASSR**		Average event-related changes in power (0–500 ms, 35-45 Hz) relative to the pre-stimulus baseline (-100~0ms)
Intertrial phase coherence (ITC) of **ASSR**		Average phase consistency (0–500 ms, 35-45 Hz) across trials and ranges between 0 (random) and 1 (identical)

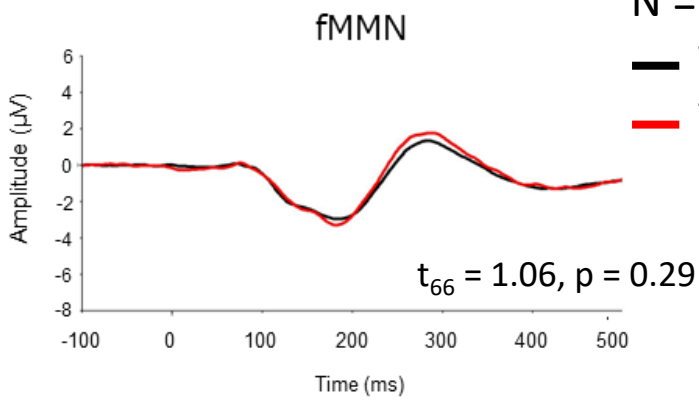
Method

Statistics

- Paried t tests (each EEG indices) ← comparison between EEG in Time 1 and in Time 2
- multiple regression analyses with stepwise method (outcome: Changes in the SDQ-TD, independent variables: changes in each EEG indices, age follow-up period) ←investigation associations between EEG and SDQ-TD
- 2 (group: high or low SDQ-TD at Time 2) × 2 (time: Time 1 or Time 2) Repeated measures ANOVA ←investigation these associations

Results: Longitudinal change of EEG indices

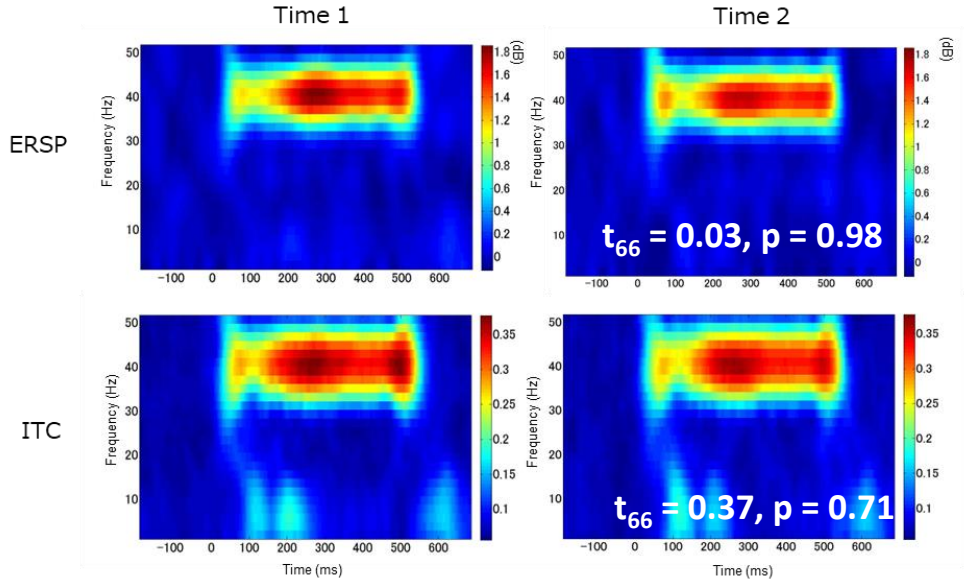




N = 67 (Girls, N = 33)

— Time 1 (13.4±0.5 years)

— Time 2 (16.1±0.8 years)

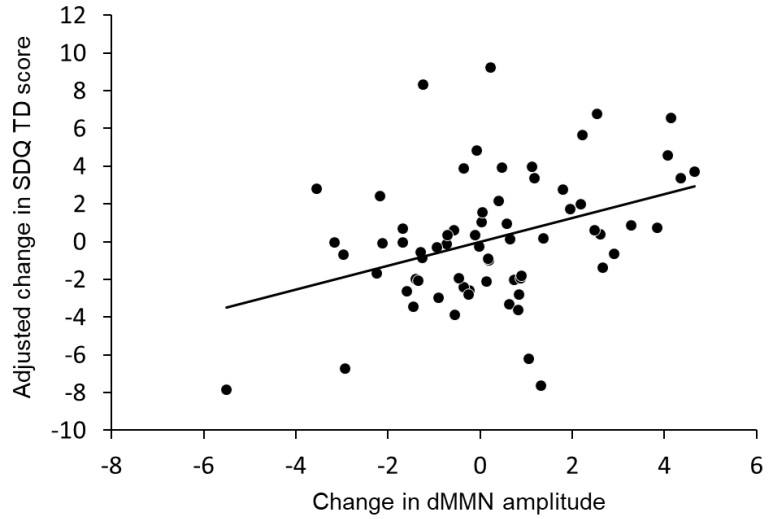


⇒all EEG indices :
no significantly change over time in the group level

Results: Relation between change in EEG and change in SDQ-TD

multiple regression analyses with a stepwise method (*p<0.05, **p<0.01)

Step	Beta	SE	F	adjusted R^2	p
Outcome: Change in SDQ-TD			5.61	0.17	0.002**
Change in duration MMN amplitude	0.36	0.20			0.003**
Sex (Girls> Boys)	−0.29	0.80			0.011*
Follow-up period	0.24	0.06			0.04*



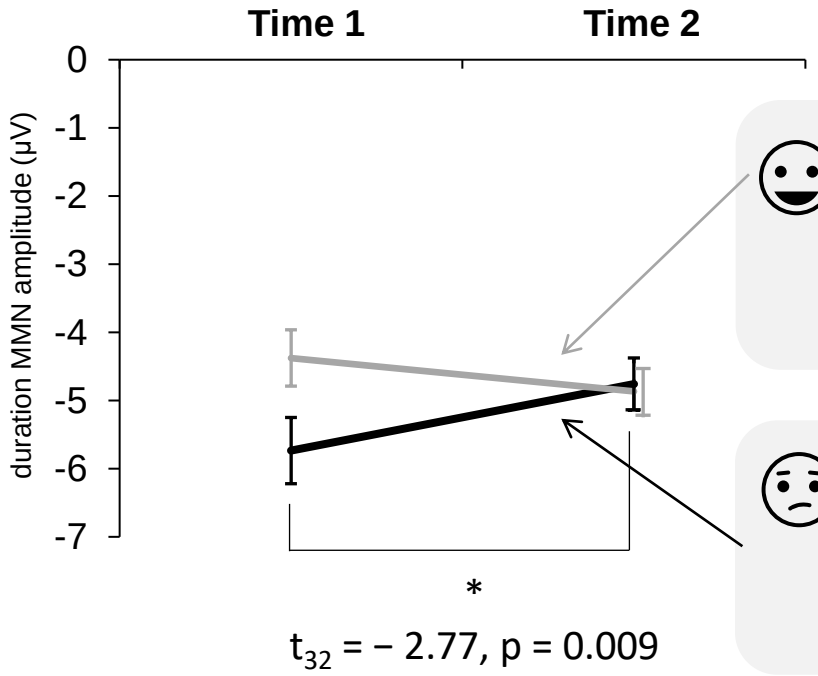
⇒significant relation of
decreased duration MMN amplitude
and
worse of psychological difficulties

Results: Relation between EEG and SDQ-TD

The result of ANOVA

significant group-by-time interaction ($F(1,65) = 10.07$, $p = 0.002$)

no significant group or time main effects ($p > 0.05$)



$t_{32} = -2.77$, $p = 0.009$

Group with **low SDQ-TD** scores (≤ 5) in Time 2 (N=34)

Low psychological difficulties

⇒ duration MMN : no change

Group with **high SDQ-TD** scores (> 5) in Time 2 (N=33)

High psychological difficulties

⇒ duration MMN : decrease

Discussion

- no significantly change of EEG indices over time

⇒ Short follow-up period (2-3 years) may influence

- Longitudinal relation between duration MMN amplitude and psychological difficulties

⇒ Longitudinal MMN attenuations are also seen in adolescents with schizophrenia antecedents (Laurence et al., 2020)

⇒ Because recent study showed that MMN reflects glutamatergic transmission,
atypical maturation of glutamatergic neurotransmission may affect psychological difficulties in mid-adolescence.