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

Kaori Usui*, Kenji Kirihara, Tsuyoshi Araki, Mariko Tada, Daisuke Koshiyama, Mao Fujioka, Ryoichi Nishimura, Shuntaro Ando, Shinsuke Koike, Kiyoto Kasai

* Department of Neuropsychiatry, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan,
Department of Community Mental Health and Law, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan
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

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

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～
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

<table>
<thead>
<tr>
<th>Indices</th>
<th>Task</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration MMN</td>
<td>Passive Oddball task</td>
<td>Average amplitude around the peak of grand-average MMN wave (± 25ms)</td>
</tr>
<tr>
<td></td>
<td>Standard stimuli (90%, 1800)</td>
<td>1000Hz, 50ms</td>
</tr>
<tr>
<td></td>
<td>Deviant stimuli (10%, 200)</td>
<td>1000Hz, 100ms</td>
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<tr>
<td></td>
<td>Frequency MMN</td>
<td>Average event-related changes in power (0–500 ms, 35-45 Hz) relative to the pre-stimulus baseline (-100~0ms)</td>
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<tr>
<td>Frequency MMN</td>
<td>Passive Oddball task</td>
<td>1000Hz, 50ms</td>
</tr>
<tr>
<td></td>
<td>Standard stimuli (90%, 1800)</td>
<td>1200Hz, 50ms</td>
</tr>
<tr>
<td></td>
<td>Deviant stimuli (10%, 200)</td>
<td>1200Hz, 50ms</td>
</tr>
<tr>
<td>Event-related spectral perturbation (ERSP) of ASSR</td>
<td>20 click/500ms = 40Hz (gamma band) sound</td>
<td>Average phase consistency (0–500 ms, 35-45 Hz) across trials and ranges between 0 (random) and 1 (identical)</td>
</tr>
</tbody>
</table>
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

\[ t_{66} = -0.94, \ p = 0.35 \]

\[ t_{66} = 1.06, \ p = 0.29 \]

⇒ 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)

<table>
<thead>
<tr>
<th>Step</th>
<th>Beta</th>
<th>SE</th>
<th>F</th>
<th>adjusted R²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome: Change in SDQ-TD</td>
<td>5.61</td>
<td>0.17</td>
<td>0.002**</td>
<td></td>
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</tr>
<tr>
<td>Change in duration MMN amplitude</td>
<td>0.36</td>
<td>0.20</td>
<td>0.003**</td>
<td></td>
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</tr>
<tr>
<td>Sex (Girls&gt;Boys)</td>
<td>–0.29</td>
<td>0.80</td>
<td>0.011*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up period</td>
<td>0.24</td>
<td>0.06</td>
<td>0.04*</td>
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</tr>
</tbody>
</table>

⇒ 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)

- **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

\[ t_{32} = -2.77, \ p = 0.009 \]
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.