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Event-related potential using task-based electroencephalogram may differentiate between mild cognitive impairment and normal controls

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Background: New non-invasive biomarkers to diagnose early Alzheimer' disease are needed. We investigated the role of event-related potential (ERP) using task-based electroencephalogram (EEG) in differentiating patients with mild cognitive problems from cognitive-normal healthy controls.

Methods: In a pilot cross-sectional study, two patients with subjective cognitive decline (SCD), two with mild cognitive impairment (MCI), and two healthy controls (HC) underwent 128-channel EEG whilst performing two cognitive tasks: go/no-go (GNG using one hand) and prospective memory (PM using two hands) paradigms. ERP components N200 and P300 were selected for GNG task, whilst N300 and parietal positivity were selected for PM task.

Results: For PM task, HC group had significantly higher parietal positivity, higher N300 mean amplitude in posterior location, and higher N300 latency than those of the MCI group. The posterior regions of the brain registered more statistically significant differences than the anterior regions, which may signify the functional neuroanatomy of the PM task. For GNG task, no significant differences in ERP were observed. Results were variable for the SCD group.

Conclusion: Our pilot results indicate that ERP using task-based EEG may have the potential to differentiate between MCI and healthy controls. Sensitivity of the prospective memory task appears to be higher than the go/no-go task, probably because it involves using two hands simultaneously, hence more challenging on the working memory and executive function.

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The C-terminal domain of hepatitis B core protein regulates hepatitis B virus transcription through recruitment of histone-modifying enzymes

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Background: The hepatitis B core protein (HBc), a component of the hepatitis B virus (HBV) covalently closed circular DNA (cccDNA) mini-chromosome, has been suggested to play a role in HBV transcription. The C-terminal domain (CTD) of HBc possesses four arginine-rich nucleic acid-binding clusters (clusters I to IV). We aimed to identify specific residue(s) or region(s) in HBc CTD essential for its interaction with cccDNA and to investigate the possible mechanism in HBV transcriptional regulation.

Methods: A total of 17 HBc CTD mutants (MT1-MT17) were created by site-directed mutagenesis. Expression plasmids containing wild-type or mutant HBc were transiently co-transfected with plasmid-free full-length HBc-negative HBV genome into HepG2-NTCP cells. HBV RNA, DNA, and HBsAg were measured by qRT-PCR, qPCR, and ELISA, respectively. The association between cccDNA and mutant HBc, as well as various histone modifying enzymes were assessed by chromatin immunoprecipitation (ChIP).

Results: Compared with wild-type HBc, HBc clusters III and IV mutants (MT6-MT17) had significantly reduced level of total HBV RNA (all $P<0.05$). All mutants had significantly lower level of intracellular encapsidated HBV DNA than wild-type HBc (all $P<0.05$). The level of secretory HBsAg of all but one HBc mutant (MT2-MT17) were significantly decreased ($P<0.05$). ChIP experiments demonstrated a relatively smaller degree of association between HBc clusters III and IV mutants and cccDNA (MT3-MT17; $P<0.05$). The relative recruitment level of histone-modifying enzymes CPB, P300, and PCAF were also lower in the HBc clusters III and IV mutants (MT7, MT12) than in the wild-type HBc (all $P<0.05$).

Conclusion: We demonstrated that HBc CTD mutants in cluster III and IV shown impaired viral transcription through their reduced association with cccDNA and the recruitment of histone-modifying enzymes, suggesting that HBc CTD clusters III and IV may be potential therapeutic target to control HBV replication.