Changes of Plasma Neurofilament Light Chain in Alcohol-dependent Patients Following Detoxification and the Effect from *ALDH2* gene

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Background

Chronic and heavy alcohol consumption can impair the brain function and cause multiple neuropathology. Blood levels of neurofilament light chain (NFL) have been suggested to be a measure of neuronal injury in neuropsychiatric disorders and recently associated with neuropsychological dysfunction in individuals with alcohol dependence (AD). In addition, alcohol is oxidized primarily by alcohol dehydrogenase to acetaldehyde, which is further metabolized by aldehyde dehydrogenase (ALDH). An *ALDH2* single nucleotide polymorphism (SNP), rs671 (A), results in significantly reduced ALDH2 enzyme activity and subsequent acetaldehyde accumulation and has been associated with neurotoxicity.

Aims & Objectives

To examine alterations of NFL levels in patients with AD during 2 weeks of detoxification and the potential of NFL to discriminate them from controls. In addition, we also determine the genetic effects *ALDH2* on the changes of NFL alcohol discontinuation.

Methods

We measured the plasma levels of NFL in 154 patients with AD and 114 age- and gender-matched healthy controls using Enzyme-linked immunosorbent assay (ELISA). We followed the NFL levels, alcohol cravings and psychological symptoms (depression and anxiety) in patients with AD after 1 and 2 weeks of detoxification. Rs671 (G→A) was genotyped in patients with AD.

Results

The baseline plasma NFL levels were significantly higher in patients with AD than controls (mean ± SD: 305.9 ± 324.1 vs. 72.1 ± 35.6pg/mL, $P < 0.001$) and were correlated with age, alcohol consumption amount and craving and anxiety severity. The NFL levels significantly reduced after one- and two-week of detoxification (190.2 ± 177.8 and 176.4 ± 161.5pg/mL, respectively). The receiver operating characteristic (ROC) curve revealed that NFL concentration of 90.8pg/mL could discriminate patients with AD from controls (area under the curve: 0.85; $p < 0.001$). The reduction of NFL levels was correlated with the improvement in craving, depression, and anxiety ($P < 0.001$). Rs671, A allele carriers, which have been associated with ALDH deficiency, displayed a more significant reduction in NFL levels compared to G allele carriers (213.4 ± 249.3 vs. 99.6 ± 179.2).

Discussion & Conclusion

We found that plasma NFL level was higher in patients with AD and the level reduced significantly after early abstinence. The reduction of NFL levels corroborated with the improvement of clinical symptoms including craving, depression, and anxiety. Interestingly, patients with less ALDH activity might restore the NFL more rapidly than the counterparts. In addition, data from the ROC curve suggests NFL may be a novel indicator for chronic alcohol consumption.