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P2-001 HELICOBACTER PYLORI FILTRATE IMPAIRS SPATIAL LEARNING AND MEMORY IN RATS AND INCREASES ß-AMYLOID BY ENHANCING EXPRESSION OF PRESENILIN-2

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Background: Helicobacter pylori (H.pylori) infection is related with a high risk of Alzheimer’s Disease (AD), but the intrinsic link between H.pylori infection and AD development is still missing. In the present study, we explored the effect of H.pylori infection on cognitive function and ß-amyloid production in rats. Methods: Twenty-seven SD rats were randomly divided into three experimental groups (n = 9) and received intraperitoneal injection of H.pylori, E.coli filtrate or the same volume of DMEM/Opti-MEM medium as control for 7 days, the spatial learning and memory ability of the rats was tested in Morris water maze; then the rats were sacrificed for ELISA detection of brain Aβ levels and Western blotting detection of expression of related proteins such as BACE-1, presenilin (PS)-1 and PS-2. The morphology of the dendritic spines was detected by Golgi staining. N2a/APP (N2a stably transfected with human APP) cells were incubated with H.pylori filtrate, E.coli filtrate or DMEM/Opti-MEM medium for 24 hours, then the Aβ levels both in the cells and media were detected by ELISA, protein levels of BACE-1, PS-1 and PS-2 in the cells were detected by Western blotting. Results: Intraperitoneal injection of H.pylori filtrate induced spatial learning and memory deficit in rats with a simultaneous retarded dendritic spine maturation in hippocampus. Injection of H.pylori filtrate significantly increased Aβ 42 both in the hippocampus and cortex, together with an increased level of presenilin-2 (PS-2), one key component of ß-secretase involved in Aβ production. Incubation of H.pylori filtrate with N2a cells which over-express APP also resulted in increased PS-2 expression and Aβ 42 overproduction. Detection of Escherichia.coli (E.coli) filtrate, another common intestinal bacterium, had no effect on cognitive function in rats and Aβ production in rats and cells. Conclusions: We conclude that soluble surface fractions of H.pylori may promote Aβ 42 formation by enhancing the activity of ß-secretase, thus induce cognitive impairment through interrupting the synaptic function.

P2-002 GENETIC CHARACTERIZATION OF BETA AMYLloid PEPTIDES IN ADULTS WITH DOWN SYNDROME WITH A FOCUS ON CHROMOSOMES OTHER THAN 21

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Background: Beta amyloid (Aβ) peptides play a critical role in the development of Alzheimer disease (AD). Adults with Down syndrome (DS) have 3 copies of chromosome 21 and overexpress genes on chromosome 21. Overexpression of the APP gene is associated with early onset of AD neuropathology and high risk for dementia. There are large individual differences in Aβ peptide levels, a wide range of age at onset of dementia and all adults with DS do not develop dementia, suggesting the importance of additional risk factors. To this end, this study focuses on the contribution of non-chromosome 21 genes that may influence Aβ peptide levels. Methods: Participants were ascertained through the developmental disability service systems of New York and neighboring states and included 261 non-demented adults with DS, 30-78 years of age at baseline. We examined tagSNPs in candidate genes using the Illumina GoldenGate custom array. Multiple linear regression was used to identify SNPs associated with differences in levels of Aβ, controlling for age, sex, intellectual disability and the APOE ε4 allele. We then performed sliding-window haplotype analysis to identify candidate haplotypes that may harbor risk variants. Results: Mean age of the participants was 49.6 ± 6.7 years; 74.4% were female. Aβ40 levels increased with age (r=0.162), while Aβ42 and the ratio of Aβ42/Aβ40 levels decreased with age (r=-0.138 and r=-0.0153, respectively). For Aβ42 levels, the strongest support was observed for rs10884341 in SORCS1 (β=4.47; p=0.02). For Aβ40 levels, risk variants in rs 7099761 and rs1187076 in IDE were positively associated (β=2.195, p=0.0001; β=2.243, p=0.0001, respectively). For Aβ42/Aβ40, rs878183 in SORCS1 was associated. Sliding window haplotype analysis revealed that two 4-SNP haplotypes starting from 94,316,828bp to 94,336,963bp were significantly associated with Aβ 40 levels after correcting for multiple tests (empirical p=0.027). For Aβ42/Aβ40 levels, haplotype starting from 108,554,591 to 108,562,008 approached significant (empirical p=0.067). For Aβ42 levels, haplotypes in SORCS1 were not significant partly due to low density coverage. Conclusions: Our results suggest that SNPs in IDE are likely to influence levels of Aβ40 in adults with DS. We are examining exome sequencing data in these candidate regions to identify risk variants.