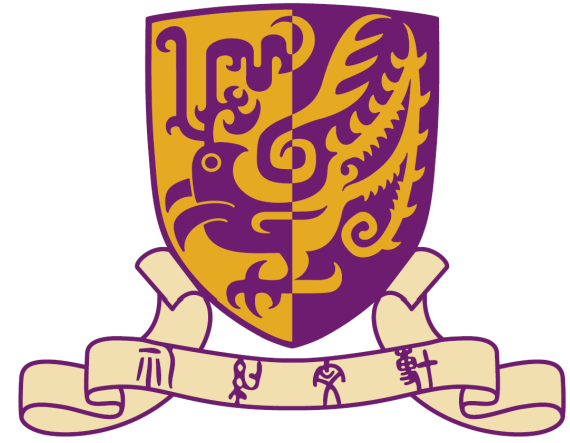


AI-empowered Retinal Imaging Analysis for Brain Health Assessment and Management in Real World Settings



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Introduction	Method
i-Cog Brain Health is a valid AI-empowered analysis of fundus photographs used for the estimation of risk of symptomatic Alzheimer’s disease (AD) in research settings. We aimed to investigate its role in screening for early symptomatic AD and for brain health assessment and management in real-world settings.	We enrolled 831 community-based cognitively unimpaired (CU) from the Brain Health Evaluation and Tailor-made Measures for Prevention of Alzheimer’s Disease (BEAT AD) study, plus 48 PET-confirmed amyloid-positive patients with early symptomatic AD (MCI, n=33; mild dementia, n=15), 27 idiopathic Parkinson’s disease (PD) patients from the brain disease, fundus photography and OCT (BRIGHT) registry. Fundus photographs were captured and uploaded to a cloud-platform for AI analysis. Results were generated within 1 minute and subjects were classified as either "positive" or "negative". Brain Health Score (BHS) was administered upon CU subjects, assessing vascular risk, physical activity, cognitive/social engagement, and diet domains, followed by nurse-led intervention consisting of tailor-made recommendation on lifestyle measures with follow-up based on individual BHS results. We calculated symptomatic AD identification probability based on screening-positive rates and investigated factors associated with positive i-Cog Brain Health results among CU subjects. In a subgroup of CU subjects with 12-month follow-up data, we examined the association between i-Cog Brain Health results and BHS changes over time.

Results

The i-Cog Brain Health positive rate among dementia patients was 66.7%, compared to 21.1% among CU subjects and 7.4% among PD patients (p<0.001). The risk of symptomatic AD was 2.81 times higher in subjects with positive i-Cog Brain Health results compared to those with negative results. Among the 831 CU subjects, those with positive results were significantly older, had lower baseline MoCA-5 scores, lower education levels, lower family income, and lower BHS. 280 CU subjects receiving the nurse-led intervention had completed 12-month follow-up. Those with positive i-Cog Brain Health results showed significantly greater improvement in BHS after age adjustment (1.8 vs 1.2, p=0.03)

	CU (n = 831)	Total early AD (n = 48)	MCI (n = 33)	Dementia (n = 15)	PD (n = 27)	Ordinal P-value	Age-adjusted P-value
Age, years	68.1 ± 5.2	68.3 ± 6.8	67.8 ± 6.0	69.3 ± 8.5	64.0 ± 10.0	< 0.001	NA
Male, n(%)	278 (33.5%)	18 (37.5%)	13 (39.4%)	5 (33.3%)	16 (59.3%)	0.046	0.055
MoCA-5	26.2 ± 2.9	17.6 ± 5.5	18.2 ± 5.0	16.2 ± 6.5	24.8 ± 2.4	< 0.001	< 0.001
i-Cog Positive, n(%)	175 (21.1%)	21 (43.8%)	11 (33.3%)	10 (66.7%)	2 (7.4%)	< 0.001	< 0.001

The flowchart illustrates the process from retinal image upload to personalized brain health optimization. It starts with 'Retinal Image' upload to a 'Cloud Platform & AI Analysis'. Results are categorized as 'Positive' or 'Negative'. 'Positive' results lead to 'Cognitive Assessment' (covering Language, Attention, Memory, Executive Function, Visual-Spatial) and 'Cognitive Impairment', which triggers a 'Biomarker Test' (Blood Pressure, LDL Cholesterol, Glucose, EMI, Smoking, Cognitive Stimulation) and 'Neuroimaging Examination' (Brain MRI, PET). 'Negative' results lead to 'Cognitive Unimpaired' and 'Modifiable Lifestyle Risk Factors Assessment' (Social Activity, Physical Activity, Diet Quality). Both paths lead to 'Personalized Brain Health Optimization Workflow', which includes 'Comprehensive Medical Assessment' and 'Tailor-made lifestyle Intervention led by nurse, therapist, other health care professionals, or digital technologies'. A final step is 'Brain Health Education' with a list of recommendations: Regular Health Monitoring, Medical Management, Cardiovascular Care, Cognitive Training, Physical Activity, and Nutritional Support. A note states: 'It is recommended to repeat i-Cog Brain Health screening and risk monitoring regularly, e.g., every 12 months for elderly individuals over 60 years old.'

Key Results

- Risk of symptomatic AD if one tests positive with i-Cog Brain Health is approximately **3 times higher** of a negative test result.
- Among cognitively unimpaired elderly subjects, i-Cog Brain Health screened out individuals that were:
 - Older
 - With lower MoCA-5
 - With lower education level
 - With lower family income
 - With more suboptimal control of modifiable lifestyle risk factors
- i-Cog screening contribute to motivating elderly subjects in lifestyle improvement.

Conclusion	Contact Information
i-Cog Brain Health effectively discriminated between CU, symptomatic AD and PD subjects in real-world settings. Among CU subjects, positive results reflected worse brain health and motivated better response from lifestyle intervention. i-Cog Brain Health enables practical community-based screening and targeted brain health management.	Dr. Yuan CAI (Vera) Email: yuancai@cuhk.edu.hk Prof. Ho Ko Email: ho.ko@cuhk.edu.hk Prof. Vincent C.T. Mok Email: vctmok@cuhk.edu.hk