Background

Type 2 Diabetes (T2D) is associated with 1 risk of Dementia. The prevalence for both conditions is alarming increasing. The risk for both diseases is higher for African Americans.

Haptoglobin (Hp) is an antioxidant produced in the Liver. Its subtypes (1-1, 2-1, 2-2) have been linked to different health outcomes in the diabetic population: Hp1-1 is associated with increased risk of stroke and white matter hyper-intensities (WMH), Hp 2-2 with MI and greater mortality.

The longitudinal study Israel Diabetes & Cognitive Decline study (IDCD) on ~1000 T2D subjects found that:

1. Hp1 carriers perform worse cognitively compared to the non-carriers.
2. Among Hp1-diabetics, poor glycemic control (ie higher HbA1c) was associated with smaller hippocampal volume and worse cognitive function.

Higher prevalence of Hp1-1 in people with African American descent (30% African American vs 14% in whites), raises the question whether Hp contributes to higher risk of dementia in African American population.

Data on 466 African American/T2D patients from ACCORD-MIND study:

1. Hp 1-1 subjects had worse cognition at baseline and declined faster.
2. Hp 2-1 subtype (specific to African American subjects) was associated with better cognition at baseline and no decline.

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The Role of Haptoglobin Genotype on Cognition in African American Elderly with Type 2 Diabetes (T2D)

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Methods

Participants (Target N= 60)

Diabetic African American, 65+, Exclude major neurological and psychiatric conditions

Assessments

1. Assessment of 4 cognitive domains: Episodic Memory, Attention/Working Memory, Semantic Categorization/Language and Executive Function as well as a global composite of the 4 domains
2. Blood Draws: Hp subtype, Apo E, Hb A1c

Depression Assessment: Geriatric Depression Scale (GDS) and Hamilton Depression Rating Scale (HDRS)

References


Progress

Recruitment

1. Clinic and community based approaches
2. Data driven EMR search and pre-approval of PCPs
3. Utilizing subjects from UDS and other studies
4. Extending the study to the VA Health System

Updated census: so far we have 14 subjects, 1 withdrew, and were excluded.

Obstacles

High exclusion rate due to stroke/ TIA

Low engagement of the Primary Physicians to approve outreach to the potential candidates

High rate of no shows

Discussion

Successful completion of the proposed study may contribute to identifying new targets for the intervention trials in dementia.

Determining the mechanism by which Hp 2-1m may confer a protective effect is particularly promising, as it could ultimately lead to therapies that protect against cognitive decline and dementia.

Future Directions

Haptoglobin

Compare the role of vascular function among different Hp subtypes (Doppler, MRI)

Comparing AD-related pathology among different Hp subtype

Longitudinal follow up of the subjects to assess trajectories of cognitive decline

Depression in diabetic patients

Subtypes of depression in T2D

Association of depression subtypes and apathy with cognitive function

Hypothesis of Hp-1 diabetics, Poor glycemic control (HbA1c) carried with more strongly associated with cognitive impairment among Hp 1-1 carriers than non carriers.

Explore the association of Hp and Depressive symptoms.

Hypothesis of Hp-1 genotype will be more strongly associated with depressed symptoms.

Figure 1. Hp1-1 subjects had worse cognitive function at baseline (a) and after the course of 48 months (b).