Retinal vascular features as a biomarker for psychiatric disorders

CHAPTER 8

SUMMARY

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Over the last few years, retinal vascular imaging has emerged as a technique to investigate microvasculature abnormalities related to the neuropsychiatric disorders. As the microvasculature in the retina and the brain share similarities in anatomy and physiology, changes in the vessels in the retina may reflect similar changes in the brain. Importantly, the imaging of the small vessels of the brain is expensive and at times invasive with current neuroimaging modalities. Retinal vascular imaging however gives a novel and unique opportunity to study the microvasculature non-invasively.

Several studies have reported an association between retinal and brain microvasculature in disorders like stroke and Alzheimer's dementia. However, retinal vascular abnormalities in neuropsychiatric conditions are underexamined. A few studies have reported abnormalities in the thickness of the retinal layers consisting of neurons viz., retinal nerve fibre layer (RNFL) in schizophrenia and bipolar disorder using Optical Coherence Tomography (OCT). The reason for thinning of these RNFL in these neurodevelopmental psychiatric disorders may be due to the common developmental origin; the retina is embryonically formed from the neural tissue. Hence the thinning of the RNFL may indicate abnormal development of the brain. However, no study has examined the retinal microvascular features in schizophrenia and bipolar disorder in comparison to healthy volunteers.

The main objective of this thesis was to investigate the use of retinal microvasculature abnormalities as biomarker for two important psychiatric disorders viz., Schizophrenia (SCZ) and Bipolar Disorder (BD) and expanding the horizon of knowledge of various parameters in the retinal imaging for finding its association with the SCZ and BD. The retinal fundus images were acquired at the National Institute of Mental Health and Neuroscience (NIMHANS), Bengaluru, India a tertiary care hospital. The summary of the thesis chapters are as below.

CHAPTER ONE gives the general introduction about psychiatric disorders and two major conditions namely SCZ and BD. This chapter includes prevalence, diagnosis and treatment of these conditions along with prevalent practices for their diagnosis. How

the retina vasculature is used as biomarker for other systemic diseases is also discussed in this chapter. The aim and outline of the thesis is described as well.

CHAPTER TWO describes the usage of retinal vascular calibre abnormalities of both veins and arteries in SCZ and BD when compared to healthy volunteers (HV). It was found that the retinal veins were significantly wider in patients when compared to HV. The retinal arteries were significantly narrower in patients when compared to HV. Interestingly, the width was larger in BD when compared to SCZ for retinal veins but the width was smaller in BD when compared to SCZ. The results were significant event after controlling for the confounding factors. The reason for such abnormalities is not known but may be due to wide range of environmental, genetic, and systemic influences such as aging, inflammation, nitric oxide–dependent endothelial dysfunction, and hypoxia/ischemia.

CHAPTER THREE investigated the usage of retinal vascular tortuosity of veins and arteries in SCZ and BD when compared with HV. The results showed significant differences across the three groups in retinal artery tortuosity but not in retinal vein tortuosity. There was significant increase in retinal arterial tortuosity in patients when compared with HV. Interestingly, there was also significant difference in SCZ and BD with BD having higher retinal arteriolar tortuosity. The results were significant even after controlling for possible confounding factors. These retinal arteriolar tortuosity can act as surrogate marker for cerebrovascular abnormalities and have value in predicting patients at risk of developing adverse cerebrovascular events.

CHAPTER FOUR studied the fractal dimension of retinal microvasculature in patients with SCZ and BD. There was a significant difference between the three groups in retinal vascular fractal dimensions. While both SCZ and BD had significantly increased fractal dimension when compared to HV, there was no significant difference between SCZ and BD. Findings remained significant even after controlling for the confounding factors. This study suggests increased possibility of adverse vascular events in SCZ and BD.

CHAPTER FIVE examines the retinal vessel trajectory as a tool for finding the abnormalities in retinal nerve fibre layer in patients with SCZ and BD when compared with HV. There was a significant difference between the groups for both retinal artery and retinal vein trajectories even after adjusting for age and sex. However, there was no significant difference between SCZ and BD. Supervised machine learning using ensembled of bagged trees was used to classify the three groups using retinal vascular trajectory measures. It showed considerably good accuracy of 86% with sensitivity of 88% and specificity of 85% for differentiating HV and SCZ. However, a lower but considerably good accuracy of 73% with sensitivity of 78% and specificity of 76% was obtained for differentiating HV and BD.

CHAPTER SIX gives the correlation between cognitive test (one back test) and the retinal vascular calibre as described in chapter 2. It was found that the performance on one back test, a test of working memory had significant positive correlation with retinal arteriolar calibre and significant negative correlation with retinal venular calibre. As anticipated, the patients (both SCZ and BD) had significantly lower working memory accuracy and higher log mean speed. This suggests the role of vascular pathology in cognitive deficits typically seen in SCZ and BD.

CHAPTER SEVEN is a discussion of important findings, issues and implications for future studies based on the above chapters.