Optical Coherence Tomography Changes in Major Depressive Disorder Patients

Thesis

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LIST OF ABBREVIATIONS

AACG	Acute angle closure glaucoma
AD	Alzheimer's disease
ADHD	Attention deficit hyperactive disorder
AMD	Age related macular degeneration
APP	Amyloid protein precursor
ASD	Autism spectrum disorder
AS-OCT	Anterior segment optical coherence tomography
Aβ	Amyloid βeta
BDI	Beck's depression inventory scale
BDNF	Brain derived neurotrophic factor
CNS	Central nervous system
CRP	C reactive protein
DSM	Diagnostic and statistical manual of mental disorders
ERG	Electroretinogram
ETDRS	Early treatment diabetic retinopathy study
GCC	ganglion cell complex
GCIP	Ganglion cell inner plexiform
GCL	Ganglion cell layer
HD	Huntington's disease
HPA	Hypothalamo-pituitary-adrenal axis
IPL	Inner plexiform layer
ipRGC	Intrinsically photopigment retinal ganglion cells
ISCEV	International society for clinical electrophysiology of vision
MD	Mean difference
MDD	Major depressive disorder
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
OCT	Optical coherence tomography
OD	Oculus Dexter
OGC	Oculogyric crisis
OS	Oculus Sinister
PD	Parkinson's disease
PERG	Pattern electroretinogram
RGCs	Retinal ganglion cells
RNFL	Retinal nerve fiber layer
RPE	Retinal pigment epithelium
SCN	Suprachiasmatic nucleus
SLD	Super luminescent diode
SNRI	Serotonin norepinephrine reuptake inhibitor
SSRI	Serotonin selective reuptake inhibitor
VLPN	Ventrolateral preoptic nucleus

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Introduction

Introduction

Major depressive disorder (MDD) is a common psychiatric disorder that affects nearly 11.1-14.6 % of the population in their lifetime **(Bromet *et al.*, 2011)**. Pathophysiology and brain imaging findings of such a prevalent and disabling disorder have received great research interest especially during recent years. Studies on the pathophysiology of major depressive disorder (MDD) show that degenerative and inflammatory processes may play a role **(Wuwongse *et al.*, 2010)**.

Meta-analysis of voxel-based morphometry studies in MDD demonstrated significant gray matter reductions in anterior cingulate cortex, dorsolateral and dorsomedial prefrontal cortex, amygdala and parahippocampal gyrus **(Bora *et al.*, 2012)**.

Furthermore, impairment of visual function is a common feature of neurodegenerative disorders, as observed in Alzheimer's and Parkinson's disease, as well as in inflammatory diseases of the CNS such as multiple sclerosis (MS) **(Schönfeldt-Lecuona *et al.*, 2017)**.

From anatomical and embryological perspectives, the retinal nerve fiber layer (RNFL), which comprises the axons of the retinal ganglion cells, can be considered a unique extension of the brain and is able to reflect axonal histopathology. Being unmyelinated, it can provide insight into the pathophysiological processes of diseases with a neurodegenerative element **(Galetta *et al.*, 2011)**.

Optical Coherence Tomography (OCT) is a non-invasive imaging method, which provides an in vivo image of the retina. It allows for

quantitative measurements of retinal and macular thickness, including single-layer analysis **(Dickmann *et al.*, 2012)**.

Studies in MDD incorporating OCT were aroused by the progressive MRI-volumetric changes in frontal and hippocampal brain regions as well as abnormalities in the visual system suggesting that the retinal structures are altered in patients with MDD **(Schönfeldt-Lecuona *et al.*, 2017)**.

Ganglion cell layer (GCL) and inner plexiform layer (IPL) were shown to have better structure-function correlation in neurodegenerative diseases such as MS than RNFL **(Saidha *et al.*, 2011)**.

To review this hypothesis, three OCT studies were performed in patients with depressive disorders **(Kalenderoglu *et al.*, 2016; Yildiz *et al.*, 2016; Schönfeldt-Lecuona *et al.*, 2017)**. However, the findings of these studies are heterogeneous and partially inconsistent, which may be partly due to methodological differences.

Also, several OCT studies showed a direct correlation between RNFL thickness and electrophysiological measurements in early stages of glaucoma and MS patients **(Parisi *et al.*, 1999, Parisi *et al.*, 2001 and Ventura *et al.*, 2006)**.

Aim of the Study

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To compare retinal optical coherence tomography parameters as retinal nerve fiber layer, ganglion cell inner plexiform layer complex, in a group of major depressive disorder patients with a healthy control group and try to find a relation between optical coherence tomography parameters and pattern electroretinography parameters in major depressive disorder patients.

Review of Literature

Chapter (1)

A Connection between Brain and Retinal Neurodegeneration

Chapter 1

A Connection between Brain and Retinal Neurodegeneration

Embryology of the retina

Like the cerebral and cerebellar cortices, the neural retina develops into a layered array of different neuronal types. Developmentally and functionally, the eye is an extension of the central nervous system **(London *et al.*, 2013)**.

In the human embryo, after formation of the neural tube and before closure of its rostral end, the optic sulci develop which later become the optic vesicles. They appear as hollow hemispherical outgrowths on each side of the embryonic forebrain vesicle **(Müller and O'Rahilly, 1985)**.

As the development proceeds, the breadth of the head increases, the future eye is now connected to the brain by the optic stalk which arises from what has differentiated into the diencephalon. The lens placode invaginates the optic vesicle to form a double layered cup **(Nag and Wadhwa, 2007)**.

The outer layer of the optic cup is formed from pseudostratified columnar ciliated epithelium. In these cells, melanogenesis starts and cilia disappear to form a single layer of hexagonal cells known as retinal pigment epithelium (RPE) by the 8^{th} week of gestation **(Bron *et al.*, 1997)**.

The differentiation of the neural retina starts earlier than the RPE from the inner layer of the optic cup. By the 33^{rd} day, the neural retina has five to six rows of neuroepithelial cells **(Rhodes, 1979)**. By the 7^{th} week, an outer nucleated two thirds of the neural retina forms the