# Neurosonologic and Cognitive Evaluation of Systemic Lupus Erythematosus Patients

***THESIS***

Submitted in the fulfillment of the M.Sc. Degree in Neurology and Psychiatry

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بِسْمِ اللهِ الرَّحْمَنِ الرَحِيم

"قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلا مَا عَلَّمْتَنَا إِنكَ

أَنْتَ الْعَلِيمُ الْحَكِيمُ"

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***Mohamed Ibrahim Raslan Hegazy***

# DEDICATION

*To my family and friends*

## Abstract

Systemic lupus erythematosus (SLE) is a common connective tissue disease that involves almost all organ systems. Involvement of the brain is one of the most important complications of SLE. About 30–70% of SLE patients develop brain involvement, which is manifested as cerebrovascular disease, seizures, cognitive disorders, headaches, and psychosis**.**

The aim of this study was to investigate whether neuropsychological dysfunction in SLE was associated alterations in CBF.

Total Cerebral Blood Flow Volume (TCBFV) was assessed by measuring flow volume of the extra cranial internal carotid and vertebral arteries using Doppler Ultrasonography and neuropsychological status was assessed by the Mini-Mental State Examination (MMSE), Modified Mini-Mental State Examination (3MS), and Ceneral health Questionaire (GHQ) in 21 SLE patients subgrouped into 10 patients with Atiphpospholipid Syndrome (Group Ia) and 11 patients without Atiphospholipid Syndrome (Group Ib) and 10 healthy volunteers.

It was found that CBFV in the Left ICA was significantly lower in patients than in controls (p value=0.05).It was also found that TCBFV was significantly lower in patients with SLE diseses activity (p value=0.006).There was no significant difference between patients and controls regarding MMSE, 3MS, or GHQ.There was no significant difference between patient subgroups regarding TCBFV, MMSE, 3MS, or GHQ.

In conclusion, cerebral hypoperfusion measured by Doppler ultrasonography was detected in patients with SLE and is related to disease activity.



**Key words:** Cerebral Blood Flow Volume; Neuropsychiatric lupus; Cognitive dysfunction; SLE Disaese Activity Index (SLEDAI).

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# List of abbreviations

| | |
|---|---|
| aCL | Anti-cardiolipin Antibodies |
| ACR | American College of Rheumatology |
| AECA | Anti-endothelial cell antibodies |
| ANA | Anti-nuclear antibodies |
| ANCA | Anti-neutrophil cytoplasmic antibodies |
| anti-b2GP1 | Anti-beta 2 glycoprotein 1 |
| anti-dsDNA | Anti-double stranded DNA antibodies |
| anti-P | Anti-ribosomal P antibody |
| aPL | Antiphospholipid Syndrome |
| BACNS | Benign angiopathy of the CNS |
| c-ANCA | Circulating antineutrophil cytoplasmic antibody |
| CBF | Cerebral blood flow |
| CBFV | Cerebral blood flow velocity |
| CBV | Cerebral blood volume |
| CNS | Central nervous system |
| CSF | Cerebrospinal fluid |
| CSS | Churg–Strauss syndrome |
| CT | Computed tomography |
| CTA | Computed tomography angiography |
| CTDs | Connective tissue disorders |
| CVDs | Cerebrovascular disorders |
| CVR | Cerebrovascular resisitance |
| DHEA | Dehydroepiandrosterone |
| DPTC | Dynamic perfusion computed tomography |
| DSCPW -MR | Dynamic susceptibility contrast perfusion-weighted magnetic resonance |
| ECD | Ethyl eysteinatedimer |
| EEG | Electroencephalography |
| ELISA | Enzyme-linked immunosorbent assay |
| ESR | Erythrocyte sedimentation rate |
| GACNS | Granulomatous angiitis of the central nervous system |
| GC | Glucose consumption |
| HBV | Hepatitis B virus |

| | |
|---|---|
| HCV | Hepatitis C virus |
| HIV | Human immunodeficiency virus |
| HMPAO | Hexamethyl propylene amine oxime |
| HSP | Henoch–Schonleinpurpura |
| ICAM-1 | Inter-Cellular Adhesion Molecule 1 |
| γIFN- | interferon-gamma |
| IgA | Immunoglobulin A |
| IgG | Immunoglobilin G |
| IL-1 | interleukin-1 |
| IL-6 | interleukin-6 |
| IVIG | intravenous immunoglobulin |
| LA | Lupus Anticoagulant |
| LCV | leukocytoclasticvasculitis |
| MAC | Membrane attack complex |
| MHC | Majorhistocompatibility complex |
| MPA | Microscopic polyangiitis |
| MPO | Myeloperoxidase |
| MRA | Magnetic resonance angiography |
| MRI | Magnetic resonance imaging |
| MS | Multiple Sclerosis |
| MTT | Mean transit time |
| NCS | Nerve conduction studies |
| NIRS | Near-infrared spectroscopy |
| NPSLE | Neuropsychiatric systemic lupus erythematosus |
| OC | Oxygen consumption |
| OEF | Oxygen extraction fraction |
| PACNS | Primary angiitis of the CNS |
| PAN | Polyarteritis Nodosa |
| p-ANCA | Perinuclear antineutrophilcytoplasmic antibody |
| PCR | Polymerase chain reaction |
| PET | Positron emission tomography |
| PMN | Polymorphonuclear leukocytes |
| PN | Peripheral sensorimotor neuropathy |
| PNS | Peripheral Nervous System |
| PR3 | Proteinase 3 |
| RCVS | Reversible cerebral vasoconstriction syndrome |
| SLE | Systemic lupus erythematosus |

| | |
|---|---|
| SLEDAI | Systemic lupus erythematosus Disease Activity Index |
| SPECT | Single photon emission computed tomography |
| SS | Sjogren syndrome |
| TA | Takayasu’sarteritis |
| TCD | Transcranial Doppler ultrasound |
| αTGF- | Transforming growth factor- alpha |
| βTGF- | - betaTransforming growth factor |
| TIAs | Transient ischemic attacks |
| TM | Transverse myelitis |
| αTNF- | Tumor necrosis factor -alpha |
| VCAM-1 | Vascular cell adhesion molecule-1 |
| VDRL | Veneral Disease Research Laboratory |
| WG | Wegener’s granulomatosis |
| XeCT | Xenon-enhanced computed tomography |

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# INTRODUCTION

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# AIM OF WORK

# Introduction and aim of work

## Introduction:

Systemic lupus erythematosus (SLE) is a chronic inflammatory multiorgan disease. It is characterized by a variety of clinical features including abnormalities of the skin, joints, lungs, heart, Kidneys, and the central nervous system (CNS). It has a variable course marked by active and inactive disease periods. The etiology of SLE is unknown, but it is believed to represent a disturbance of the immune system, leading to influence of or damage to various organs. Involvement of the brain – neuropsychiatric SLE (NPSLE) – is one of the most important manifestations, reportedly ranging from 20% to 75% of cases (McCune and Golbus 1988 ;Futrell et al.,1992).

The CNS findings vary from global to focal cerebral dysfunction (Omdal et al., 1989) and the main features are cerebrovascular disease seizures, cerebral atrophy, psychosis, headaches, cognitive abnormalities and mood disorder. Unlike many other organ manifestations, the pathophysiology underlying CNS disease is not clear (van Dam ,1991).The observation of both diffuse and focal CNS involvement in SLE has led to the hypothesis that there are several pathogenetic mechanisms in NPSLE such as microvascular damage, small vessel vasculopathy and autoantibody mediated neuronal cell injury (Devinsky et al.,1988; Hanly et al.,1992).It has been proposed that about two-thirds of neurological manifestations in SLE are not related to the disease itself, but result from associated

causes, such as drugs, infection, and hypertensive and metabolic complications( Kaell et al.,1986

Transcranial color Doppler sonography (TCCD) is a useful tool for intracranial investigation. It provides direct sonographic imaging of intracranial vessels and brain parenchyma. It is also a noninvasive, reproducible and bedside mobile device for evaluating the cerebral hemodynamics, including blood flow direction, flow velocities, and other abnormal vascular lesions (Lin et al., 1995)

Neuropsychological assessment is another method of evaluating brain function (Lezak , 1995 ;Reitan and Wolfson 1993). Neuropsychological testing evaluates the functional capacity of the human brain. Assessing cognitive function has been proposed as a sensitive tool for investigating NPSLE and cognitive dysfunction has been reported in a high proportion of SLE patients (Denburg et al., 1987 ; Hanly et al.,1992; Kozora et al.,1998)

# Aim of the work

The purpose of this study was to screen cerebral perfusion by establishing Total Cerebral Blood Flow Volume (TCBFV) by using Doppler Ultrasonography and determining whether a relationship exists between cerebral hypoperfusion, cognitive dysfunction, cumulative tissue damage and the clinical activity of SLE.