

## Psychological Factors Associated with Central Serous Chorioretinopathy

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### Abstract

Central serous chorioretinopathy (CSC), characterized by serous detachment of the macula, is a clinically important retinal disease presenting as various visual symptoms. Predisposing psychopathological factors have been investigated and psychological stress, specific personality profiles and psychiatric disorders were suggested as relevant factors. These psychic factors induce hormonal changes by stimulating the sympathetic nervous system, thus aggravating the extravasation of the serous fluid from choroid. Psychotherapeutic strategies may be a significant treatment modality for CSC patients.

**Keywords:** Central serous chorioretinopathy; Psychopathology; Stress; Type A behavior, Personality trait; Psychotherapy

Central serous chorioretinopathy (CSC) is a relatively common posterior segment disease characterized by serous detachment of the neurosensory retina. Altered function of the retinal pigment epithelium (RPE) and choroidal vascular hyperpermeability suggestive of choroidal vascular compromise have been thought to play important roles in the pathogenesis of CSC [1,2]. CSC typically affects middle aged adults between 30 and 50 years and is more prevalent in men, with the peak annual incidence in men being between the years 35 and 39 [3,4]. Patients with CSC may experience sudden onset of blurred vision, metamorphopsia, decreased color vision and central scotoma. While acute CSC usually resolves spontaneously within 2-6 months, the chronic subtype with recurrent or persistent episodes may result in permanent visual loss with structural RPE damage [5,6].

The etiology and pathophysiology of CSC has yet to be completely understood. Previous investigations have suggested various genetic, biological and environmental predisposing factors associated with CSC. Recent studies have reported possible risk single nucleotide polymorphisms (SNPs) related to CSC [7-9]. Systemic cardiovascular diseases and hypertension has also been proposed as a potential risk factor in previous studies [10,11]. Endocrine changes in pregnancy and Cushing syndrome are related to CSC development [12]. Exogenous steroids use has been reported to aggravate subretinal fluid accumulation in CSC patients throughout numerous studies from past to present [13-15]. Nonetheless, one of the most important predisposing factors yet to be described and investigated in detail are the psychopathological features such as specific personality traits, psychological stress, and psychiatric illness [16-33].

In 1986, Yannuzzi proposed an association between CSC and type A personality [16]. Type A behavioral characteristics imply elevated competitiveness, aggressiveness, relentless, impatience, a sense of time urgency and an easily aroused temperament [16]. Yannuzzi's study suggested patients chosen to have a type A behavioral pattern showed highly significant difference in the incidence rate of CSC compared to that of the control group. Previously, several authors had made reference to emotional disturbances as a causative factor in the pathogenesis of CSC. Horniker first proposed that psychic disturbances induce retinal angiospasm and secondary exudative change in the macula [17]. Harrington and Zelig suggested that anxiety precipitates autonomic vasomotor instability, which is another pathogenic model of CSC [18]. Thereafter other papers have focused on emotional distress, higher anticipatory anxiety levels, inadequate coping strategies with psychological stress, poor quality of life (QoL) status, and psychiatric disorders [19-28].

Various psychometric instruments have been used to objectively evaluate and measure psychological distress. These include the Symptom Checklist 90-R consisting of nine primary symptom dimensions (somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) with global severity index (GSI) score, the Coping with Stress Questionnaire Stressverarbeitungsfragebogen (SVF 78) [29], the Freiburg Personality Inventory (FPI-R) [30], the Hamilton Anxiety Rating Scale (HAM-A) [31], the Temperament and Character Inventory (TCI) [32], and Short Form-36 (SF-36) [33].

Conrad et al. suggested that emotional distress and specific aspects of type A personality behavior is related to CSC [19,20]. CSC patients are expected to be impulsive, impatient, easily bored, pessimistic and emotionally unstable. The subscale levels for somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility and paranoid ideation were increased in CSC patients. However, there was no association between visual acuity or the time since onset of symptoms and emotional distress. Another study by Conrad et al. [21] proposed that personality traits with competitiveness, hostility and emotional detachment, lower level of cooperativeness, and reward dependence are distinctive patterns of CSC patients. Stressful life events in workplace and uncontrolled stress coping have a role in CSC, with patients characterized as being ambitious overachievers, perseverant and hard-working [22,23]. Moreover, emotional distress and high level of anxiety can appear as somatic complaints such as general weakness, gastrointestinal pains, high heart rate and arterial hypertension and respiratory symptoms [24,25]. These kinds of psychological status in CSC patients leads to overall lower quality of life compared to control groups [26], and the tendency to experience psychiatric disorders such as schizophrenia, depression, hysteria, psychopathic deviance and hypochondriasis was increased in CSC patients [27]. The association

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between critical life events (unemployment, financial problem, familial and partnership issues) and CSC development is controversial. Conrad et al. [20] revealed no significant relationship between critical life events and CSC, but a recent study from Greece suggests a potential impact of economic crisis on CSC development [28].

The hypothesis of psychopathologic effects on CSC is that these unfavorable psychic factors accumulate and influence endogenous hormonal status. Increased levels of stress hormones such as corticosteroids and catecholamines have been found to induce CSC [34,35]. Cloninger et al. [32] suggested specific temperament dimensions; low reward dependence, low cooperativeness, emotionally detached; show increased level of norepinephrine in the locus coeruleus, which are closely associated with type A behavior patterns. The interaction of stress hormones triggers sympathetic nervous stimulation, vasomotor instability, and activates adrenergic receptors within the vascular bed of the choroid. The innermost layer of the choroid, Bruch's membrane weakens and allows serous fluid to extravasate from the choriocapillaris under the macula, thus causing serous retinal pigment epithelial detachment. Furthermore, in the central nervous system, hypothalamic-pituitary-adrenal (HPA) axis dysregulation and mineralocorticoid participates in stressful condition, which is observed in psychiatric illness such as depression [36].

The retina is sequestered from the systemic circulation. The retina has two barrier components which prevent certain substances and fluid from entering the retina; the inner retinal vascular endothelium and the outer RPE. Elevated circulating cortisol and epinephrine are thought to affect the autoregulation of the choroidal circulation. Endogenous corticosteroids in stressful conditions affect both the glucocorticoid and mineralocorticoid receptor and hydro-ionic homeostasis in RPE cells and retinal Muller glial cells are impaired by corticosteroids [37]. Therefore, the balance in retinal hydration is damaged by stress hormones which activate microglial cells in the RPE layer and induces RPE inflammation [38]. RPE inflammation then promotes both choroidal vasodilation and RPE barrier rupture. As a result, fluid accumulates under the retina, leading to CSC development.

The hypothesis of mineralocorticoid receptor pathway activation in CSC has been studied in experimental rat models [39]. Intraocular injections of aldosterone or high-dose corticosterone (the endogenous glucocorticoid hormone in rodents) showed enhanced expression of the water channel aquaporin-4 (AQP4) and sodium/potassium ion channels. These mineralocorticoid receptor over-expressed rats provoked choroidal vasodilation and leakage, increased choroidal thickness, endothelial dysregulation, RPE tight junctions disruption and resulted in RPE detachments and subretinal fluid formation.

For treatment of CSC, laser photocoagulation, verteporfin photodynamic therapy (PDT), anti-vascular endothelial growth factor (anti-VEGF) intravitreal injection and oral medications (carbonic anhydrase inhibitors, beta-blockers) are widely used. Mineralocorticoid receptor antagonists such as oral spironolactone and eplerenone have been investigated [40]. Since psychological distress and type A personality characteristics influence the development of CSC, CSC patients may benefit from psychoeducation and psychosocial support or interventions. Recent meta-analysis revealed that psychodynamic therapy and cognitive behavior therapy proved to be effective treatments for depression and personality disorders [41]. Pharmacologic regulators of sympathetic agents also can be helpful for the treatment and prevention of CSC. Such psychotherapeutic methods can be fundamental strategies for the cure of CSC.

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