reflex activity) shows a decrease during deep breathing (Ulas *et al.*, 2006). The amplitude of SSR recorded from the palmar, plantar and genital regions is reduced in the patients with FM, indicating both autonomic and sexual dysfunction (Unlü *et al.*, 2006).

Exercise modulates autonomic function in fibromyalgia

Exercise training in patients with fibromyalgia is well documented, and tailored aerobic or mixed-type training programmes reduce pain and depression and improve physical fitness (Jones *et al.*, 2008; Staud *et al.*, 2010; Busch *et al.*, 2011; Kayo *et al.*, 2012). Both prescribed graded aerobic and resistance exercise regimens evoke improvements in FMS-specific symptoms (tender points and FIQ scores), depression and global SF-36 (Short Form Health Survey 36) scores (Richards & Scott, 2002; Sañudo *et al.*, 2010). Exercise in a warmwater (34°C) pool provides additional beneficial effects on pain, depression and anxiety compared with land exercise performed in a gymnasium (Jentoft *et al.*, 2001). Pool-aquatic exercise in warm water decreases high circulating levels of the pro-inflammatory marker IL-8, which is specifically associated with increased nociception and activation of sympathetic nervous system (Staud, 2007; Ortega *et al.*, 2009).

The patients with FM perceive repetitive isometric exercise more painful and show attenuated adrenaline responses along with higher muscle activity (Giske *et al.*, 2008). Resistance exercise training (RET) results in a greater parasympathetic (total power, HF and root mean of squared successive RR Intervals) modulation of HRV and improves pain perception in patients with FM (Figueroa *et al.*, 2008). Baroreflex sensitivity is not affected by RET because increased arterial stiffness (evident by high pulse pressure) reduces the stimulation of the baroreceptors in patients with FM (Figueroa *et al.*, 2008). FM patients with a normal autonomic profile at rest, after an acute bout of resistance exercise, demonstrate a lower sympathetic reactivity and greater parasympathetic (high HF; impaired vagal withdrawal that persists during recovery in postexercise phase) modulation. In the same study, a higher BRS with a normal HR recovery postexercise suggests reduced autonomic responses and a reduced sensitivity of sinus node to autonomic modulation, respectively. These changes, however, pose a low cardiac risk after acute resistance exercise in patients with FM (Kingsley *et al.*, 2009). But no evidence of HRV modulation after an acute bout of leg resistance exercise is found in patients with FM who have undergone RET for 12 weeks and heart rate recovers in 20 min postexercise (Kingsley *et al.*, 2010). Patients with FM on a different exercise protocol show a delayed heart rate recovery postexercise, which may predispose patients to cardiovascular risk. Patients with FM undergoing endurance exercise (modified Balke treadmill maximal exercise test) show chronotropic incompetence (the inability to increase heart rate with an increase in exercise intensity), indicating sympathetic hyporeactivity and cardiac autonomic impairment (da Cunha Ribeiro *et al.*, 2011). A blunted HR response during exercise is because of desensitization of cardiac β1-receptors through a heightened baseline sympathetic activity (Martinez-Lavin, 2004). A high HR response in patients with FM during the static muscular contraction leading to a higher HR at exhaustion is attributed to deconditioning as evident with a low baroreflex control of HR (Kadetoff & Kosek, 2007).

Muscle blood flow in Patients with FM

A Doppler ultrasound reveals a blunted increase in muscular vascularity (duration and immediate flow response) following dynamic and during static muscular contractions which can be explained on the basis of deconditioning and derangement of the sympathetic nervous system and/or pain-related muscle ischaemia (Elvin *et al.*, 2006). Propranolol increases the sensitivity to pain induced by arm ischaemia in patients with FM, suggesting that a greater α-adrenergic activation induces higher vasoconstriction and BP and produces myalgic pain through hypoperfusion. This reinforces existing knowledge about disturbed microcirculation in patients with FM (Light *et al.*, 2009; Kulshreshtha *et al.*, 2012a).

Vascular end organ in patients with fibromyalgia

Amitriptyline therapy (most common conventional pharmacological treatment for FM) improves blood flow at the affected sites in patients with FM. This local action of amitriptyline corroborates fibromyalgia as a case of vascular end organ dysfunction (Kulshreshtha *et al.*, 2012) Amitriptyline, through the blockade of α_1-adrenoceptors/extracellular calcium influx through voltage-gated calcium channels, induces relaxation of the isolated mesenteric vasculature and results in the dilatation of resistance vessels in healthy subjects (Thorstrand & Lindblad, 1976; Vila *et al.*, 1999).

Vascular smooth muscle cells (VMC) express β-receptors for vasodilation and α_1-/α_2-adrenoceptors for vasoconstriction. Activation of endothelial α_2-adrenoceptor by the release of NE from the sympathetic nerve terminals (which terminate in medial VMC layer) releases NO causing endothelium-dependent vasodilation (Guimarães & Moura, 2001; Pintérová *et al.*, 2011). Endothelial-derived signals and physical factors, such as hypoxia and stretching, stimulate vascular sensory afferents, and resultant activity in the efferent vasomotor nerve causes the release of catecholamines from the varicosities (Stohler, 2002). High sympathetic outflow and endothelial dysfunction pose a higher detrimental cardiovascular risk than either of them alone. Impaired endothelial function enhances the contractile function of catecholamines (Joyner & Green, 2009). Exaggerated sympathetic activation impairs endothelial function via α-/β-receptors whose blockade results in the restoration of flow-mediated dilation (FMD) and lessens the