Table of contents

Perspectives

The importance of sympathetic activity in regulation of blood pressure in undeniable, however a primary role of sympathetic activity in development of hypertension as well as in blood pressure responses to training is unclear and ambiguous. To elucidate the role of sympathetic activity in hypertension, studies are needed that correct for age, body composition, disease progression and severity of blood pressure increase. The appealing idea that increased sympathetic activity leads to hypertension and that training is able to decrease sympathetic activity and therefore reduce hypertension, lacks evidence. The regulation of vascular tone is multifactorial and becomes increasingly difficult to explain when investigated in a dynamic situation i.e. exercise, during sympatho-excitement etc. One area in need of further investigation, in particular, is β-adrenoceptor vasodilation, that can perhaps add to the body of knowledge on vascular function and regulation. The studies presented in this thesis only had male participants. Seeing how there are known differences in male and female vascular regulation, future studies should asses the role of sympathetic activity, pannexin-1 channel and colchicine in women.

Summary

Hypertension is a lifestyle-related disease affecting more than 1 billion adults and contributes to the death of 9.4 million people each year. Exercise training is able to reduce resting blood pressure in hypertension and while sympathetic activity is increased in hypertensive individuals, the relationship between training induced reductions in blood pressure and changes in resting muscle sympathetic nerve activity is poorly understood. The pannexin-1 channel has been proven to be potentiate sympathetic vasoconstriction but has not been investigated in relation to hypertension

nor training-induced reductions in blood pressure. Large cohort studies have suggested beneficial effects of the anti-inflammatory drug colchicine in hypertensive individuals. Colchicine has also been shown to have microtubule-disrupting effects leading to increased β-adrenergic vasodilation in rodent studies. This thesis includes results from two intervention studies in normotensive and hypertensive middle-aged men; one study investigating the effect of an 8-week period of intense aerobic cycle training on skeletal muscle microvascular function and muscle sympathetic nerve activity, hereunder the involvement of the pannexin-1 channel; and one study examining the acute and 3 week daily treatment with colchicine effect on beta adrenoreceptor sensitivity. Based on the results it is concluded that changes in resting muscle sympathetic nerve activity is unlikely to explain training-induced blood pressure reductions in hypertensive individuals. Furthermore the effect of the pannexin-1 channel is not increased in hypertensive individuals neither is the pannexin-1 channel able to explain training induced reductions in blood pressure in hypertensive individuals. Lastly, colchicine increases β-adrenergic and NO-mediated vasodilation in hypertensive individuals confirming the suggested transient mechanism of action of the drug, previously reported in rodent studies. The role of sympathetic activity in vascular regulation is complex, multifaceted and yet to be fully elucidated.

Resumé

Hypertension er en livsstilsrelateret sygdom som mere end 1 milliard voksne lider af og som årligt er skyld i 9,4 mio. dødsfald. Træning kan sænke blodtrykket i hypertension og selvom sympatisk nerveaktivitet i hvile er forhøjet hos hypertensive individer, er sammenhængen mellem træningsinducerede blodtryksfald og ændringer i sympatiske nerve-aktivitetsmålinger i hvile ikke undersøgt grundigt. Det er blevet foreslået at pannexin-1 kanalen har en forstærkende effekt af sympatisk vasokonstriktion, men dette er ikke blevet studeret i relation til hypertension eller træningsinducerede fald i blodtryk. Større kohorte-studier har set en positiv effekt af det anti-inflammatoriske lægemiddel Colchicine hos hypertensive individer. Studier har desuden vist at colchicine splitter mikrotubuli og forårsager β-adrenerg vasodilatation i studier på gnavere. Denne afhandling inkluderer resultater fra to interventionsstudier i normotensive- og hypertensive midaldrende mænd; ét studie undersøgte effekten af 8 ugers højintens spinning-træning på mikrovaskulær funktion i skeletmuskulatur og sympatisk nerveaktivitet til musklerne, herunder involvering af pannexin-1 kanalen, mens et andet studie undersøgte effekten af akut og 3 ugers daglig behandling med colchicin på β-adrenerg vasodilatation. På baggrund af resultaterne konkluderes det, at ændringer i sympatisk nerveaktivitet til musklerne ikke kan forklare træningsinducerede reduktioner i blodtrykket hos hypertensive individer. Derudover er betydningen af pannexin-1 kanelen ikke øget hos hypertensive individer og pannexin-1 kanalen kan ikke forklare træningsinducerede reduktioner i blodtrykket hos hypertensive individer. Slutteligt øger colchicine β-adrenerg og NO-medieret vasodilatation, hvilket bekræfter den foreslåede forbigående effekt af lægemidlet der tidligere er rapporteret hos gnavere.