

**BLOOMFIELD EARLY CAREER PROFESSORSHIP  
IN CARDIOVASCULAR RESEARCH**

**Brain-derived neurotrophic factor, a novel hypothalamic mediator in hypertension**

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**LAY SUMMARY**

Psychological stress, high fat and high salt diets are all well recognized risk factors for hypertension and cardiovascular diseases. Compelling evidence also indicate a potential synergy between these risk factors augmenting each other's hypertensive effects due to alterations in central blood pressure regulatory mechanisms. The neurotrophin peptide, *brain-derived neurotrophic factor (BDNF)* is a well-known regulator of neuronal function in the central nervous system, and BDNF production has been shown to increase markedly in the hypothalamus during stress, and in response to high dietary salt, fat and calorie intake. Interestingly, our recent studies indicate that BDNF, acting in the hypothalamus, is an important regulator of cardiovascular function that increases sympathetic nervous system activity and elevates blood pressure. Therefore, in this proposal, we will test the hypothesis that hypothalamic BDNF signaling mediates the synergistic hypertensive effects of stress, high salt intake and high fat/high calorie diets. Using transgenic mice, hypothalamic microinjections of viral vectors and radiotelemetric blood pressure measurement, we will specifically test whether inhibition of BDNF synthesis in the hypothalamus reduces blood pressure increases to stress, high salt and high fat/high calorie diets and prevents facilitation of hypertensive responses when these challenges are applied in combination. In addition, using optogenetics, we will directly test how inhibition of BDNF synthesis affects firing activity of hypothalamic neurons and their influence on cardiovascular function. The proposed studies will significantly further our understanding of hypothalamic blood pressure regulatory mechanisms and may help to identify novel therapeutic targets to treat hypertension.