The effects of thermal discomfort on health and human performance were investigated in an office, in an attempt to elucidate the physiological mechanisms involved. Twelve subjects (six men and six women) performed neurobehavioral tests and tasks typical of office work while thermally neutral (at 22°C) and while warm (at 30°C). Multiple physiological measurements and subjective assessment were made. The results show that when the subjects felt warm, they assessed the air quality to be worse, reported increased intensity of many sick building syndrome symptoms, expressed more negative mood, and were less willing to exert effort. Task performance decreased when the subjects felt warm. Their heart rate, respiratory ventilation, and end-tidal partial pressure of carbon dioxide increased significantly, and their arterial oxygen saturation decreased. Tear film quality was found to be significantly reduced at the higher temperature when they felt warm. No effects were observed on salivary biomarkers (alpha-amylase and cortisol). The present results imply that the negative effects on health and performance that occur when people feel thermally warm at raised temperatures are caused by physiological mechanisms.