For the clarification of the response of baroreflex-governed sympathetic outflow in humans to microgravity (μG), changes in muscle sympathetic nerve activity (MSNA) leading to antigravity muscle were examined, and the effects of breathing maneuvers were assessed during μG produced by parabolic flight. MSNA was microneurographically measured from the tibial nerve of sitting humans (n=10) with their legs extended in a jet aircraft. MSNA was recorded simultaneously with the electrocardiogram, the blood pressure wave by Finapres, the respiration curve, and the thoracic fluid volume by impedance plethysmography. In half of the parabolas, their breathing was controlled at 0.25 Hz using a metronome, and other trials were under natural respiration. At the entry to hypergravity (hyper-G) at 2 G just before μG, the thoracic fluid volume was reduced and the blood pressure was lowered, which caused the enhancement of MSNA. At the entry to μG, the thoracic fluid volume was increased, which elevated the systemic blood pressure and suppressed the MSNA. However, this suppression lasted only approximately 10 sec, followed by an enhancement of MSNA which continued for several seconds in natural breathing trial. The suppression was more marked with controlled than with uncontrolled respiration (51.6 ± 7.2 vs 82.8 ± 2.5 %, mean ± SE, 1G = 100%). The blood pressure fall 10 to 16 sec after μG entry was less prominent with controlled than with uncontrolled respiration. Heart rate changes were significantly suppressed, and significantly less elevated during μG. We conclude that MSNA is suppressed and then enhanced during μG produced by parabolic flight. These changes in MSNA are in response not only to intrathoracic fluid volume changes but also to arterial blood pressure changes, both of which are caused by body fluid shifts induced by parabolic flight, and these changes are quite phasic and transient. Another conclusion for the breathing effect is that less changes in arterial blood pressure during μG might be a main cause in more suppressed MSNA and heart rate during μG with controlled respiration, and the breathing maneuver might provide a clue to lessen the unpleasant feeling during gravitational change.