The Space Flight Cognitive Assessment Tool for Windows (WinSCAT) is a computer-based, self-administered battery of five cognitive assessment tests developed for medical operations at NASA’s Johnson Space Center in Houston, Texas. WinSCAT is a medical requirement for U.S. long-duration astronauts and has been implemented with U.S. astronauts from one NASA/Mir mission (NASA-7 mission) and all expeditions to date on the International Space Station (ISS). Its purpose is to provide ISS crew surgeons with an objective clinical tool after an unexpected traumatic event, a medical condition, or the cumulative effects of space flight that could negatively affect an astronaut’s cognitive status and threaten mission success. WinSCAT was recently updated to add network capability to support a 6-person crew on the station support computers. Additionally, WinSCAT Version 2.0.28 has increased difficulty of items in Mathematics, increased number of items in Match-to-Sample, incorporates a moving rather than a fixed baseline, and implements stricter interpretation rules. ISS performance data were assessed to compare initial to modified interpretation rules for detecting potential changes in cognitive functioning during space flight. WinSCAT tests are routinely taken monthly during an ISS mission. Performance data from these ISS missions do not indicate significant cognitive decrements due to microgravity/space flight alone but have shown decrements. Applying the newly derived rules to ISS data results in a number of off-nominal performances at various times during and after flight. Correlation to actual events is needed, but possible explanations for off-nominal performances could include actual physical factors such as toxic exposure, medication effects, or fatigue; emotional factors including stress from the mission or life events; or failure to exert adequate effort on the tests.