Oral appliance therapy is emerging as an alternative to continuous positive airway pressure for the treatment of obstructive sleep apnea (OSA). However, its precise mechanisms of action are yet to be defined. We examined the effect of a mandibular advancement splint (MAS) on upper airway collapsibility during sleep in OSA. Ten patients with proven OSA had a custom-made MAS incrementally adjusted during an acclimatization period until the maximum comfortable limit of mandibular advancement was reached. Polysomnography with the splint was then performed. After a 1-week washout period, upper airway closing pressures during sleep (with and without MAS) were determined. Significant improvements with MAS therapy were seen in the apnea/hypopnea index (25.0 +/- 3.1 vs. 13.2 +/- 4.5/hour, p < 0.03) and upper airway closing pressure in Stage 2 sleep (-1.6 +/- 0.4 vs. -3.9 +/- 0.6 cm H2O, p < 0.01) and in slow wave sleep (-2.5 +/- 0.7 vs. -4.7 +/- 0.6 cm H2O, p < 0.02) compared with no therapy. **These preliminary data indicate that MAS therapy is associated with improved upper airway collapsibility during sleep.** The mediators of this effect remain to be determined.