Note-taking is an activity that all college students engage in, and with many options available to them, it is hypothesized that factors such as perceived hand fatigue or desired notetaking rationale have an influence in a student's choice. Note-taking methods include handwritten via pen/paper, handwritten via stylus/tablet, or typing via computer/keyboard. This study consists of a two-part multimethod design which includes quantitative and qualitative data gathered from undergraduate students at a Southeastern US university. The survey includes questions about note-taking methods, perceptions of hand fatigue, and note-taking rationale which provide quantitative data. Semi-structured interviews provided qualitative data. The purpose of this study is to understand the factors that influence a student's choice of note-taking method, specifically through perceived hand fatigue associated with the method of note-taking, note-taking rationale associated with the method of note-taking, or some other factor. Of the 24 respondents, the most preferred note-taking method was handwriting via stylus/tablet (n=13). Higher rates of perceived hand fatigue (on a scale from 6-30, with higher scores representing higher perceived hand fatigue) were reported for handwriting notes via pen/paper (mean±SD =  $18.5\pm5.6$ ) vs. typing notes via computer/keyboard (mean $\pm$ SD =  $11.5\pm6.4$ ; P<0.001). Also, the mean±SD score for handwriting via stylus/tablet was 15.3±4.8 and did not statistically differ from the other two note-taking methods. No statistical differences in note-taking rationale were found between preferred note-taking methods as related to speed (P=0.26), organization (P>0.99), legibility (P=0.50), and recall of information (P>0.99). Lastly, among those participating in semi-structured interviews, themes related to note-taking via stylus/tablet emphasized the importance of downloading PowerPoint slides for annotation during lecture. Because the study yielded a small sample size, further investigation is needed to determine the social factors that influence choice of note-taking methods in this population.