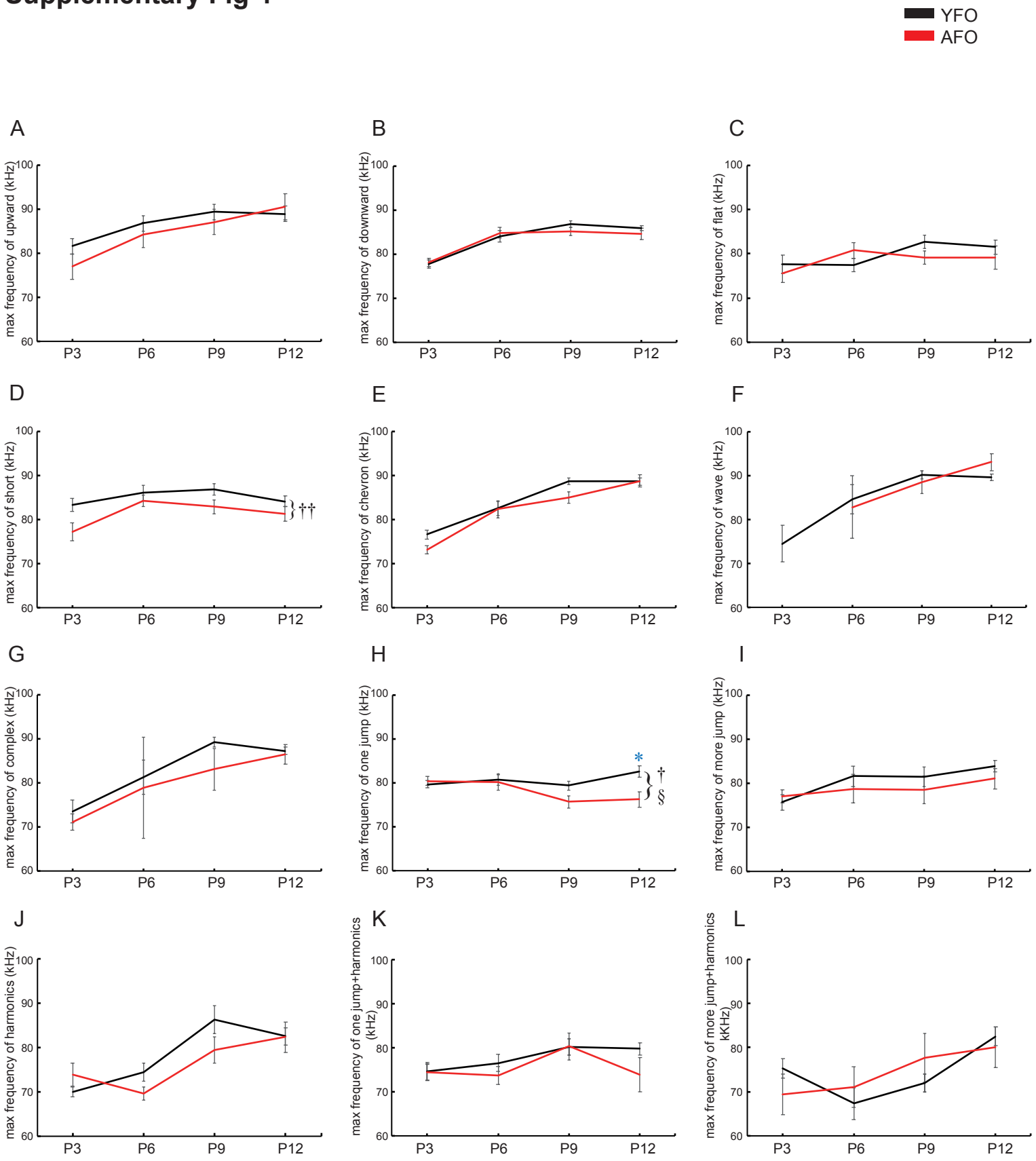Supplementary Fig 4