Transcranial magnetic stimulation (TMS) of the human primary motor hand area (M1-HAND) can produce multiple descending volleys in fast-conducting corticospinal neurons, especially so-called indirect waves (I-waves) resulting from trans-synaptic excitation. Facilitatory interaction between these I-waves can be studied non-invasively using a paired-pulse paradigm referred to as short-interval intracortical facilitation (SICF). We examined whether SICF depends on waveform and current direction of the TMS pulses. In young healthy volunteers, we applied single- and paired-pulse TMS to M1-HAND. We probed SICF by pairs of monophasic or half-sine pulses at suprathreshold stimulation intensity and inter-stimulus intervals (ISIs) between 1.0 and 5.0 ms. For monophasic paired-pulse stimulation, both pulses had either a posterior-anterior (PA) or anterior-posterior (AP) current direction (AP-AP or PA-PA), whereas current direction was reversed between first and second pulse for half-sine paired-pulse stimulation (PA-AP and AP-PA). Monophasic AP-AP stimulation resulted in stronger early SICF at 1.4 ms relative to late SICF at 2.8 and 4.4 ms, whereas monophasic PA-PA stimulation produced SICF of comparable size at all three peaks. With half-sine stimulation the third SICF peak was reduced for PA-AP current orientation compared with AP-PA. SICF elicited using monophasic as well as half-sine
pulses is affected by current direction at clearly suprathreshold intensities. The impact of current orientation is stronger for monophasic compared with half-sine pulses. The direction-specific effect of paired-pulse TMS on the strength of early versus late SICF shows that different cortical circuits mediate early and late SICF.