**Optimal Experimental Design for Alternating Event related fMRI Designs**

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 Functional Magnetic Resonance Imaging (fMRI) measuring the BOLD signal is a remarkable tool for visualizing human brain activity. But the BOLD signal is slow and sluggish, being delay seconds after the corresponding neural event(s). This presents special challenges for the design and analysis of event-related fMRI studies, which must optimize statistical efficiency – the accuracy with which a hemodynamic response evoked due to one event type can be detected and estimated – in a limited amount of imaging time. For some cognitive designs, the challenges are significant, for example in designs where the events occur in a fixed sequence, like a trial-by-trial cue-target paradigm (e.g., attention cuing paradigms), where the power of event randomization cannot be employed. Using the package *fmrisim* (Ellis et al., 2020, PeerJ), we investigated the dependence of efficiency on several design parameters: Stimulus Onset Asynchrony (SOA), frequency of events, and inclusion of semi null trials (e.g., cues not following by targets). The use of shorter SOAs decrease the efficiency of detecting a signal. However, the most efficient design for detecting a response is not the best one to estimate the shape of the response, which is better with longer SOAs (minimizing overlap). Finally, we show that the inclusion of semi-null trials in the event sequence can facilitate the estimation efficiency as opposed to detection power. The goal here was to utilize the simulation power of *fmrisim* to understand how the varying design parameters could be optimized to minimize the estimation of overlapping events in a fixed sequence design.