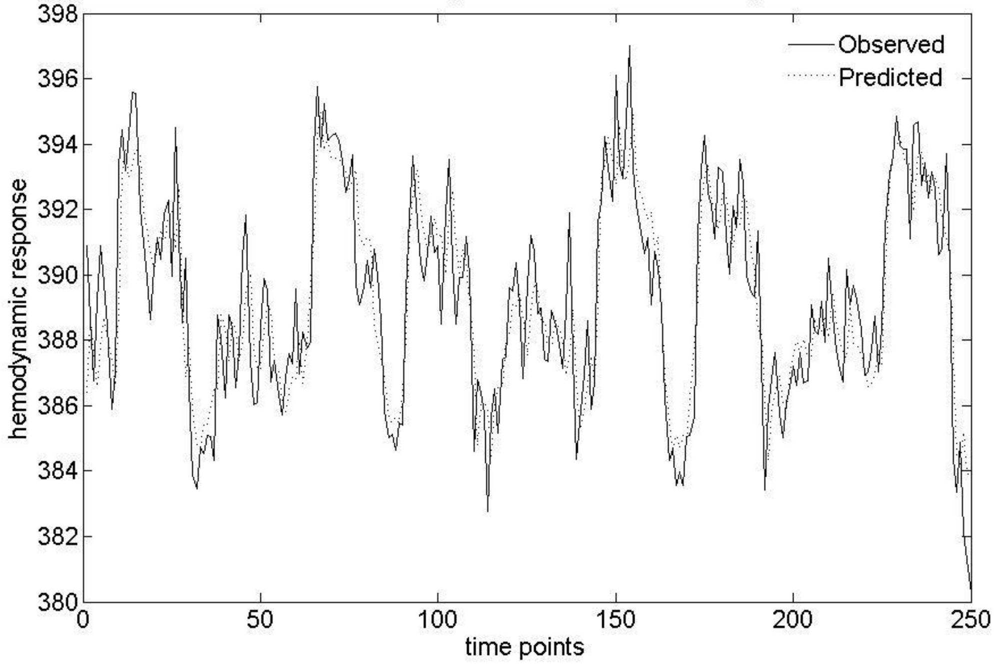
Introduction: To optimize blocked fMRI experiments, we applied methods from optimal design theory, e.g. the D-optimality criterion and the maximin criterion, which had not been applied before in fMRI research. The maximin criterion determines the optimal design for experiments with unknown parameters, e.g. here unknown correlation in the fMRI data time series. Our objective was to determine optimal block length, stimulus onset asynchrony (SOA) and block order for a blocked experiment with fixed total scanner time.

Methods: The general linear model was used to describe the fMRI signal at one voxel to two stimulus types. The model included a baseline effect, two stimuli effects and one linear trend effect. Assuming linearity of the hemodynamic response function (HRF) and a double gamma function as HRF, the design matrix was derived. An autoregressive error of order 1 (AR1) was used to describe temporally correlated noise. Our assumptions for the HRF and an AR1 structure were checked by analyzing the data from a blocked experiment. The fit of our predicted time course can be seen in Figure 1.

Figure 1) Observed time course from blocked experiment and predicted time course from general linear model based on double gamma function and autoregressive error of order 1



Different SOAs, block lengths and orders were considered, thereby modeling a variety of blocked designs. The following values were considered:
- SOA of 1, 2, and 3s
- block length of 10, 15, 20, 30 and 60s
- block order AB, ABN, ANBN (A indicating a block of stimulus A, B a block of stimulus B, N a null/rest block)

Thus, 45 designs were compared.

We used several optimality criteria (D-, A-, D_s-, A_S- and c-optimality criterion) to reflect different research questions, e.g. estimation of all effects (D,A), estimation of stimulus effects (D_S, A_S) and estimation of a differential contrast between stimuli A and B (c).

Optimal designs depended on the autocorrelation parameter for the error structure and therefore the maximin approach based on a relative efficiency measure was considered to handle this so-called local optimality problem.

For each design, its relative efficiency with the locally optimal design was computed for given values of autocorrelation, and its minimum relative efficiency was then determined. The maximin

design is the design with highest minimum relative efficiency over all designs and thereby robust against misspecification of the autocorrelation.
Analyses were performed with MATLAB (The MathWorks Inc., Natick, MA).

Results: The maximin design for all optimality criteria had block length (BL) 15 s and an SOA of 1 s. For the D-, D_S- and A_S-optimality criteria the maximin design had block order ABN, for the A-optimality criterion ANBN and for the c-optimality criterion AB. Locally optimal designs had BLs of 15 s or 20 s depending on the amount of correlation. Block length had a small effect on minimal relative efficiency whereas block order and SOA had a stronger effect. Results can be seen in Figure 2 and 3 which show the minimal relative efficiencies for all designs and criteria.

Conclusions:
A block length of 15 seconds and the use of null blocks can be recommended to estimate precisely and robustly all or some of the effects. To estimate the difference between two stimulus effects precisely, no null blocks should be applied. The SOA should be as small as practically possible.

Figure 2) Minimal relative efficiencies. MMD denotes the maximin design.

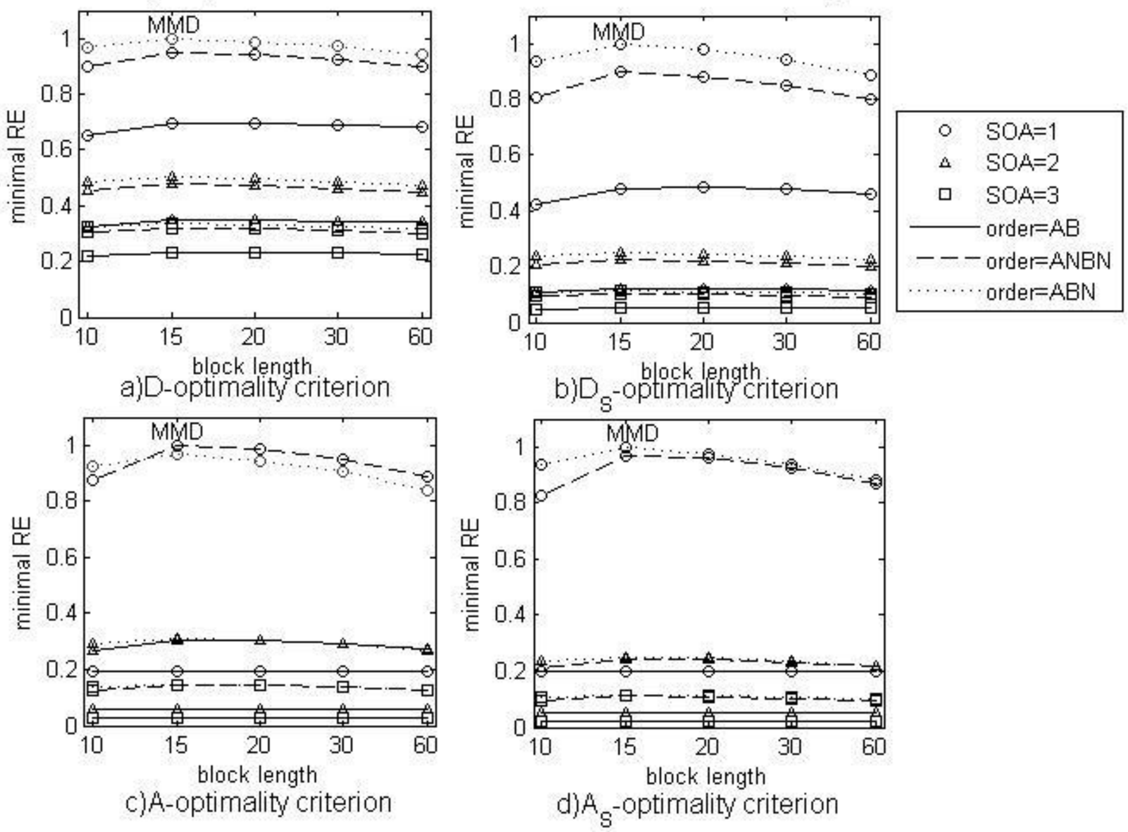


Figure 3) Minimal relative efficiencies for c-criterion.
MMD denotes the maximin design.