Identification of biomarkers suitable for predicting cognitive decline in patients undergoing cardiac surgery

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Introduction

• Postoperative cognitive decline (POCD) remains significantly high in patients undergoing cardiac surgery1,2
• At discharge, 50-80% of patients exhibit POCD, persisting in 20-50% of patients 6 weeks after surgery3.
• Currently available cerebral oximeters (e.g. INVOS) that use near-infrared spectroscopy (NIRS) for patient monitoring are based on small-area, low-density arrays
• Utilize declines in cerebral hemoglobin saturation (Hbsat / rSO2) to predict POCD
• Demonstrated poor sensitivity4
• We hypothesize that large, high-density arrays (HDA) of NIRS probes, used in combination with biomarkers based on cerebral autoregulation, will provide better predictions of POCD

Methods

• 17 patients undergoing elective cardiac surgery
• Patients performed neurocognitive tests before surgery and at time of discharge.
  - Trail Making Part A & B
  - Grooved Pegboard
  - Symbol Digit Modalities
• MMSE: Animal naming. Short story recall from Community Screening Interview for Dementia
• Modified Word List Learning
• 20% decrease in performance in at least 2 of the tests was considered to be a POCD5
• Intra-operatively, patients monitored with HDA of 48 optical sources and 32 detectors
• HDA arranged into 104 overlapping source-detector pairs (channels), inter-optode distance of 4cm - Figure 1
• Several biomarkers (Results) derived from NIRS data were tested using rank-sum tests to differentiate those with and without POCD
• Biomarkers were tested using smaller partial arrays to determine if a smaller system can be used in the future.

Results

• 11 out of 17 patients able to complete pre and post-operative testing and had NIRS and mean arterial pressure (MAP) data suitable for analysis
• ARRAYS ANALYZED – values of each biomarker were averaged across a given array for each patient (Figure 2 identifies each partial array location with colored dots)
  • Global: All good channels for a given patient (ranges from 19 to 103)
  • HbSat < 65%: the number of time frames that met the threshold (65%)
  • 12 good: the 12 channels that had good data quality for all 17 patients
• Forehead: An 8-channel array with optodes over the forehead region
• INVOS-mimic: a 2-channel array located over the forehead in a position similar to that used by INVOS.
• BIOMARKERS ANALYZED – values derived from the NIRS data that were used in attempts to separate patients with and without POCD
  • Sat < 65%: the number of time frames when saturation fell below 65%
  • Sat< < 20%: the number of time frames when saturation or HbT fell more than 20% of the baseline value
  • Autoreg: The number of overlapping 5-minute intervals (i.e., minutes 0-5, 1-6, 2-7...) with Pearson correlation between HbTsat and MAP > 0.46
• High correlation implies a loss of autoregulation - Figure 3
  • Total-MAP: analogous to Autoreg but utilizing HbT instead
• Autoregulatory marker distinguishes the groups, for ALL arrays
• Use of subtraction-based statistical correction methods produce a reduction in statistical significance

Conclusions

• Correlation-based autoregulatory markers are easy to obtain and can differentiate those with and without POCD
• Superficial correction methods are not needed
• RM ANCOVA analysis: Forehead array demonstrated significant results after covarying for age and surgery duration
• Only a small inter-group effect due to age or surgery duration
• Small, but high-density forehead array may provide best balance between ease-of-use and data quantity
• Autoregulation may be dependent on rate of change of MAP as well as its absolute level
• More study needed

References


Repeated Measures ANCOVA

• Performed using each partial array as a repeated measure, with patient age or duration of surgery as a covariate
• p-values are reported for one-tailed tests; a priori hypothesis is that number of autoregulatory failures cannot be higher in patients who do not develop POCD.
• Autoregulatory marker of the forehead array after adjusting for age has a large effect (ηp² = 0.36); compare to the small effect for age (ηp² = 0.02)

Autoregulatory marker with age (d.f. = 1,11)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Global F</th>
<th>p = 0.06</th>
<th>Forehead F</th>
<th>p = 0.034</th>
</tr>
</thead>
<tbody>
<tr>
<td>INVOS-mimic</td>
<td>F = 0.69</td>
<td>p = 0.22</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Autoregulatory marker with surgery duration (d.f. = 1,11)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Global F</th>
<th>p = 0.04</th>
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<tbody>
<tr>
<td>INVOS-mimic</td>
<td>F = 0.43</td>
<td>p = 0.12</td>
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</table>

Table 1: Biomarker values and p values for differences between the patient groups (rank-sum testing).

Table 2: Output from the repeated measures ANCOVA, using age or surgery duration as a covariate.