Accuracy of clinical signs, SEP, and EEG in predicting outcome of hypoxic coma: a meta-analysis
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CRD summary
This review concluded that sensory evoked potential was marginally better than the absence of motor response for predicting outcome after hypoxic coma; this superiority diminished after day one and when no motor response, decerebrate or decorticate postures were used. Some caution is warranted when interpreting the conclusions due to a lack of quality assessment and some study details.

Authors' objectives
To compare motor and pupillary responses with sensory evoked potential and electroencephalography (EEG) for predicting outcomes after hypoxic coma.

Searching
PubMed and EMBASE were searched between January 1966 and December 2007 for articles published in English, German and French; search terms were reported. Reference lists of relevant articles were searched.

Study selection
Retrospective and prospective studies in adults with anoxic-ischaemic coma secondary to cardiac arrest, respiratory failure, drowning or hypotensive shock were eligible for inclusion. Patients with coma secondary to stroke, trauma, intracranial infection, sepsis and metabolic dysfunction, or those with hypothermia were excluded. Studies had to report the timing of assessment and eventual clinical outcomes. Primary review outcomes were severe neurologic deficit, persistent vegetative state or death.

Most studies included patients with hypoxic coma secondary to cardiac arrest only; other studies had other causes of coma such as respiratory insufficiency, severe hypotension, postoperative coma, carbon monoxide poisoning and drowning. Where reported, mean patient age ranged from 41 to 72 years.

One reviewer selected the studies.

Assessment of study quality
No formal validity assessment was performed.

Data extraction
Results for positive and negative test results and the occurrence or not of clinical outcomes were extracted as 2x2 tables by the timing of the test (within 24 hours of coma onset or during days two and three). These were used to calculate sensitivity and specificity.

Data were extracted by two reviewers. Disagreements were resolved by discussion with a third reviewer.

Methods of synthesis
Summary receiver operating curves (SROC) were created for each test and the area under the curve (AUC) was calculated. M1 from the Glasgow Coma scale (denotes absence of motor response) was used as a reference test and AUCs of other tests were compared to this. Huber-White variance estimates were used to account for possible correlation between test results (some studies performed several tests on the same patients) and these were used to calculate 95% confidence intervals (CIs). A further analysis using a random effects model was used to assess the impact of statistical heterogeneity on the results.

Results of the review
Twenty-five studies (n=2,360) were included: 18 prospective studies, two retrospective studies and five were unclear. Six studies reported that treatment decisions were made blind to the test results.

Clinical outcomes within 24 hours of coma onset: Sensory evoked potential had the best diagnostic accuracy (AUC 0.891) for predicting poor outcomes and this was the only test to have significantly greater accuracy than M1 (absence of motor response, difference in AUC 0.105, 95% CI 0.023 to 0.187). AUC for other tests were: 0.805 for M≤3 (no motor response, decerebrate or decorticate postures), 0.744 for absent pupillary response, 0.837 for burst suppression or isoelectric EEG findings and 0.786 for M1.

Clinical outcomes during days two and three: M≤3 had the best diagnostic accuracy (AUC 0.948) for predicting poor outcomes and this was the only test to have significantly greater accuracy than M1 (difference in AUC 0.074, 95% CI 0.007 to 0.141). AUC for other tests were: 0.825 for absent pupillary response, 0.800 for burst suppression or isoelectric EEG findings, 0.912 for sensory evoked potential and 0.874 for M1.

Authors' conclusions
Sensory evoked potential was marginally better than M1 for predicting outcome after hypoxic coma, but this superiority diminished after day one and when M≤3 was used. Therefore, these findings caution against the generalisation that sensory evoked potential was a better marker than clinical signs.

CRD commentary
This review specified clear inclusion criteria for the participants and outcomes, but broad criteria for study design (essentially any type was allowed). The search covered two main databases, but was restricted to three languages so there were risks of language and publication biases. Data were extracted by two reviewers, but it seems that only one person selected the studies which may have introduced possible bias into the review. Other than assessing whether treatment decisions were made blind to test results, there was no assessment of study quality. The designs of the included studies were unclear other than they were prospective or retrospective. SROC analysis was used and this was appropriate, but it was difficult to tell which curves belonged to which tests on the published figures. Additional data were reported as available in a online table (unable to access to verify content).

Some caution is warranted when interpreting the conclusions of this review due to the lack of both quality assessment and detail of individual study results.

Implications of the review for practice and research
Practice: The authors stated that SEP was only marginally better than motor signs and its use in clinical practice should reflect this, especially in settings such as rural or underdeveloped settings where SEP was not widely available (in these contexts, a careful clinical examination should be used). Caution should be used for use of SEP in settings where clinical signs were unreliable when patients were under the influence of sedative medicines, anaesthetic agents or muscle relaxants.

Research: The authors stated that further studies were needed to validate the prognostic accuracy of clinical and electrophysical tests in patients treated with induced hypothermia.

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