Published in final edited form as:

J Head Trauma Rehabil. 2016 ; 31(3): E49–E59. doi:10.1097/HTR.0000000000000163.

NEUROCOGNITIVE MODELS OF MEDICAL DECISION MAKING CAPACITY IN TRAUMATIC BRAIN INJURY ACROSS INJURY SEVERITY

Kristen L. Triebel, PsyD¹, Thomas A. Novack, PhD², Richard Kennedy, MD, PhD³, Roy C. Martin, PhD¹, Laura E. Dreer, PhD⁴, Rema Raman, PhD⁵, and Daniel C. Marson, JD, PhD¹

¹Department of Neurology, Division of Neuropsychology, University of Alabama at Birmingham (UAB), Birmingham, AL

²Department of Physical Medicine and Rehabilitation, UAB, Birmingham, AL

³Division of Gerontology, Geriatrics and Palliative Care, Department of Medicine, UAB, Birmingham, AL

⁴Department of Ophthalmology, UAB, Birmingham, AL

⁵Department of Family and Preventive Medicine, UCSD, San Diego, CA

INTRODUCTION

Traumatic brain injury (TBI) can have a profound impact on a person's capacity to function independently in everyday life¹⁻⁴. A capacity that has particular functional, ethical, and legal importance in TBI is the capacity to make treatment decisions (medical decision-making capacity, or MDC). MDC is a fundamental aspect of personal autonomy and self-determination⁵. Soon after their injury, TBI patients are confronted with numerous medical decisions, such as the treatment of brain trauma and orthopedic injuries, rehabilitation programming, managing or changing medications, and the use of advanced directives⁶. Patients with TBI often experience sudden impairment or loss of MDC after injury, and this impairment may continue during rehabilitation and afterwards⁴. Although MDC impairment is greater in patients with moderate/severe TBI, some patients with mild TBI demonstrate impaired consent capacity⁷.

Neurocognitive impairment is a defining aspect of most TBI injuries. Common impairments include memory retrieval deficits, executive dysfunction, slowed information processing speed, language dysfunction, and reduced attention and concentration⁸. Empirical evidence has shown that these cognitive impairments are associated with poor functional outcomes such as return to work⁹, managing finances¹⁰, and driving¹¹. Neuropsychological predictor studies can improve our knowledge of the relationships between neurocognitive functioning

Corresponding Author: Daniel C. Marson, J.D., Ph.D., Department of Neurology, University of Alabama at Birmingham, Sparks Center 650, 1720 7th Avenue South, Birmingham, Alabama 35294-0017. Phone: (205) 934-2334, Fax: (205) 975-3094. dmarson@uab.edu.

Financial Disclosure: Dr. Marson receives income from royalties paid to the UAB Research Foundation for the Capacity to Consent to Treatment Instrument.

and decisional capacity in TBI. Clinically, such studies can be used to alert healthcare providers to specific neurocognitive impairments that threaten consent capacity and facilitate use of interventions (e.g., enhanced consent procedures) to support the decision making ability of impaired patient populations^{12, 13}.

Our research group has previously investigated MDC in patients with moderate/severe TBI^{4, 7} and with mild TBI⁷. These studies have revealed that MDC is impaired in patients with complicated mild TBI and moderate/severe TBI one month following injury. Previous research with a different sample of patients with moderate/severe TBI showed that greater short-term verbal memory predicted greater consent capacity around the time of acute inpatient hospitalization for patients with moderate/severe TBI.⁶ At six-month follow-up, however, greater executive functioning and working memory were associated with greater MDC in patients with TBI. An unresolved research question concerns the neurocognitive mechanisms associated with MDC performance in patients with milder cases of TBI.

In the present study, we examined neurocognitive predictors of MDC in cognitively healthy adults and in patients with mild and moderate/severe TBI evaluated within 6 weeks of injury using an established capacity assessment instrument (Capacity to Consent to Treatment Instrument (CCTI)). Separate neurocognitive models of MDC were identified for controls, patients with mild TBI, and patients with moderate/severe TBI. Based on prior findings in patients with moderate/severe TBI, we hypothesized that measures of memory would be key baseline predictors of performance on the different CCTI consent standards across groups. We also hypothesized that different cognitive models of consent capacity would emerge for the two TBI groups due to their different neurocognitive profiles.

METHODS

Participants

Sixty healthy adult controls and 104 patients with recent TBI were prospectively enrolled between October 2007 and October 2011 as part of a National Institutes of Health funded longitudinal study investigating medical decision-making capacity in patients with TBI. We recruited participants with TBI from the emergency department, inpatient neurosurgery, inpatient trauma, and inpatient rehabilitation services at an academic medical center, and from an outpatient neurospine service. Consistent with the protocol established by the TBI Model Systems program, participants were initially assessed within a window of 2 to 6 weeks after injury, with a goal of assessing at one month after injury¹⁴. Evaluating at a fixed interval after injury provides a more accurate appraisal of the effects of the injury across subjects.

The study research team reviewed all potential participants with TBI in order to determine if they met the following eligibility criteria: (a) documented brain injury (severity levels described below) caused by an external mechanical force accompanied by loss of consciousness (LOC), PTA, or objective neurological findings uncovered during the physical or mental status exams that could be reasonably attributed to TBI¹⁵ (persons with penetrating brain injury were not eligible); (b) evaluation within 6 week period post-injury; (c) participants were 19 years of age or older; (d) participants provided informed research

consent or had a legal guardian who could provide consent; (e) participants could communicate verbally; and (f) participants had no history of learning disability, CNS neurological disorders, prior moderate or severe TBI (individuals with a history of prior mild TBI occurring at least one year before enrollment were still eligible), alcohol or drug abuse within a year of study participation (established by patient or collateral report or medical records), or severe psychiatric disturbance.

Enrolled participants with TBI were also assigned a TBI injury severity level by a board-certified neuropsychologist with specialization in TBI and rehabilitation (T.A.N.). In this study, mild TBI (mTBI) was classified as an injury resulting in Glasgow Coma Scale (GCS) score between 13 and 15¹⁶, and LOC <30 minutes or PTA that was less than 24 hours. Participants meeting this criteria for mTBI who also had intracranial abnormalities on conventional computed tomography (CT) scans but who did not require surgical intervention (i.e., complicated mild TBI¹⁷) were included in the mTBI group.

Moderate/severe TBI was defined as an injury involving a GCS score <12 and LOC>30 minutes or PTA duration > 24 hours^{16, 18, 19}. When information about severity of injury was incongruent, more weight was given to the GCS score than to LOC or PTA when making classification determinations. The GCS score was viewed as an objective measure collected close to the time of injury, whereas duration of LOC and PTA were viewed to more subjective ratings (particularly for the more mildly injured participants). For example, if a person had a GCS score of 12 but PTA less than 24 hours, that person would be classified as moderate/severe rather than mild.

Sixty control participants were recruited from the community through local advertisements. Eligibility criteria for controls were the same as for TBI participants with the exception there was no prior history of TBI (per self-report).

Group matching was used to match controls with TBI patients on age, years of education, gender, and ethnicity. We did not try to match the mild TBI and moderate-severe TBI participants, but rather enrolled all persons with TBI who met the eligibility criteria.

Procedures

Written informed consent was obtained from each participant or in some cases their authorized legal representative. If during the course of the study consent process, there was concern that the participant could not comprehend the study information being presented to them, or the referring physician raised a concern about the person's consent capacity, then research consent was obtained from a family member who held legal power of attorney and assent was obtained from the participant. Research consent capacity was not formally assessed in this study. The institutional review board approved this study.

All enrolled TBI patients were capable of participating in the cognitive evaluation as judged (when necessary) by the study neuropsychologist, although not all patients had achieved full orientation at the time of the baseline assessment. All participants completed the study's consent capacity measure and a battery of neuropsychological measures.

Measures

Consent Capacity Measure—Treatment consent capacity was assessed using the Capacity to Consent to Treatment Instrument (CCTI)²⁰, a conceptually based, reliable and valid psychometric instrument for assessing MDC in both healthy and cognitively impaired adults^{20, 21}. The CCTI includes two clinical vignettes that each present a hypothetical medical problem and symptoms (A: neoplasm and B: cardiovascular disease), and two treatment alternatives with associated risks and benefits. Participants then answer standardized questions designed to assess each of the following four core consent standards (Ss) derived from the medical and legal literature^{20, 22}:

S1: simply expressing a treatment choice (*expressing choice*);

S3: appreciating the personal consequences of a treatment choice (*appreciation*);

S4: providing rational reasons for a treatment choice (*reasoning*); and

S5: understanding the treatment situation, available treatment choices, and respective risks/benefits of the treatment choices (*understanding*).

A fifth standard [S2] measures the ability to make a *reasonable treatment choice*²⁰. [S2] is considered an experimental consent standard because of the potential arbitrariness of the operative term “reasonable.” Therefore, brackets are used to distinguish [S2] from the other four core consent standards.

The two CCTI vignettes were read aloud and also simultaneously presented in written form to all participants. After presentation of a vignette, the written format was removed and participants responded to verbal questions tapping the five CCTI standards. Trained research assistants administered the CCTI and neuropsychological test battery, and scoring the protocols following detailed and well-operationalized criteria²⁰. Administration of the CCTI was audio-taped and subsequently transcribed to ensure a high level of scoring accuracy. Research assistants were blinded to participants’ group status and the study investigators were not involved in the CCTI administration or scoring.

Neuropsychological Test Variables—All participants were administered a standardized battery of neuropsychological tests relevant to cognitive impairment in TBI and associated with consent capacity^{8, 12}. In order to control for scaling differences among individual cognitive tests, we used factor analysis to create cognitive composite scores with individual test scores assigned to specific factor domains. A four-factor solution was optimal in terms of model fit. The four cognitive domains and constituent tests were as follows:

(1) processing speed/executive function (Trail Making Test Part A and B²³, Digit Symbol Coding and Symbol Search subtests from the Wechsler Adult Intelligence Scale-Revised (WAIS-III)²⁴;

(2) academic achievement (WAIS-III Arithmetic, WTAR Reading Wechsler Test of Adult Reading; WTAR)²⁵;

(3) verbal fluency (animal fluency, fruit/vegetable fluency, and clothing fluency²⁶); and

(4) memory (California Verbal Learning Test, second edition [CVLT-II]²⁷ [Trials 1-5 total recall, short delay free recall, and long-delay free recall], Logical Memory I and II (immediate and delayed recall) subtest of the Wechsler Memory Scale, third edition (WMS-III)²⁸.

Raw neuropsychological test scores were transformed into age, and when available, education adjusted scaled scores using published test normative data using test manuals cited above. Individual test scaled scores that comprised a given domain were averaged to yield the domain scaled score. Participants missing >50% of the individual test scores in a domain were excluded from analyses. For participants missing less than 50% of the individual test scores in a domain, we averaged the available test scores.

The CVLT-II Forced Choice was administered to assess effort/test validity²⁷.

Data Analyses

We analyzed demographic variables using one-way ANOVA (age, years of education, GCS score, and Galveston Orientation and Amnesia Test [GOAT] score²⁹) or Pearson's chi square tests (gender and race). For each CCTI standard, scores from vignette A and B were summed to create a composite variable (except for *reasonable choice*, which is unique to vignette A). Group comparisons on these composite CCTI variables and cognitive variables were performed using ANOVA (S5) or χ^2 analysis (*reasonable choice*). Post-hoc analyses for significant omnibus test findings were performed using Bonferroni multiple comparisons test or pairwise χ^2 analyses.

We examined bivariate correlations between demographic, clinical variables (age, years of education, race/ethnicity, gender, GOAT score), and cognitive domain scores with the CCTI standard scores. The purpose of this analysis was to examine associations between demographic and clinical variables with CCTI consent standard performance.

We next analyzed the relationships between the cognitive domain scores and the CCTI scores. We used ordinary least squares regression models to examine the association between cognitive domain scores and S5 (*understanding*), and ordinal regression to examine the association between domain scores and the odds of higher scores on S3 (*appreciation*) and S4 (*reasoning*). There was little score variance on the elementary and less clinically relevant standards of *evidencing choice* (S1) and *reasonable choice* [S2] and these standards were not further analyzed.

Separate regression analyses were performed for each group (e.g., controls, mTBI, and msevTBI). All four neuropsychological domain scores were simultaneously entered into the regression equation for each standard. The proportional odds assumption was evaluated using the test of parallel lines and by comparing the observed and expected cell counts at each threshold; no substantial deviations from proportional odds were observed. Model fit was measured using R^2 and adjusted R^2 for the S5 model, and goodness of fit test and Nagelkerke pseudo- R^2 ³⁰ for S3 and S4. For S3 and S4, we analyzed odds ratios and the 95% confidence intervals around them for cognitive variables that were significant in the models.

Secondary analyses were run examining bivariate correlations between CCTI standard scores (S5-S3) and the cognitive domain scores separately for complicated and uncomplicated mild TBI cases. In addition, to examine the relationship between test-taking effort as measured by the CVLT-II Forced Choice test and CCTI performance, we performed a linear regression analysis in which the four neuropsychological domain scores and the CVLT-II Forced Choice score were simultaneously entered as independent predictors, and S5 score was the dependent variable.

Significance level was set at .05 (two-sided). Statistical Package for the Social Sciences (SPSS for Mac OS X, version 22.0) was used for all statistical analyses.

RESULTS

Sample Characteristics

Based on study criteria, 104 patients with TBI were enrolled of which 49 had recent mild TBI (mTBI) and 55 recent moderate/severe TBI (msevTBI). Among the 49 participants with mTBI, 21 met criteria for complicated mild TBI based on positive CT findings. Mean time from date of brain injury to date of study evaluation (baseline) was 32.4 days (SD=12.2 days). In the msevTBI group, we recruited 54 (98.2%) participants from the UAB inpatient rehabilitation service and 1 (1.8%) participant from the neurosurgery service. In the mTBI group, we recruited 19 (38.8%) from the emergency department, 12 (24.5%) from neurosurgery, 10 (20.4%) from inpatient rehabilitation, 7 (14.3%) from trauma, and 1 (2%) from the neurospine services.

Demographic and TBI injury severity variables for all participants are presented in Table 1. Groups did not differ in age, years of education, or racial distribution. There was a gender difference with significantly more men in the msevTBI group compared to control and mTBI groups. As expected, patients with msevTBI had significantly lower GOAT and GCS scores than patients with mTBI. Of 52 msevTBI cases with available GOAT scores, 19 (36.5%) performed at or below 75 on the GOAT at baseline assessment.

CCTI Performance Results

Table 2 displays CCTI performance of the three groups. Controls and mTBI patients performed better than patients with msevTBI on all five consent standards. Controls also performed better than the mTBI patients on the *appreciation* (S3) and *understanding* (S5) standards.

Performance on Composite Cognitive Measures

Controls performed better than mTBI patients on all four composite cognitive measures. Controls and mTBI patients performed better than the msevTBI patients on all four composite cognitive measures (Table 3).

Relationships between Clinical and Demographic Variables and CCTI Consent Abilities

We examined bivariate correlations between CCTI standard performance and demographic and clinical variables. There were no significant associations between the CCTI consent

standards and age, gender, education, or race/ethnicity. For both TBI groups, there was a significant association between level of orientation and CCTI performance, as higher scores on the GOAT were associated with higher scores on the CCTI standards.

Cognitive Predictors of CCTI Consent Abilities

Using OLS regression (S5) and ordinal regression (S3-S4), we analyzed the relationship between the cognitive composite scores and each of the three clinical CCTI standards for each group. For all of the S5 analyses, a positive relationship indicated that higher (better) scores on the cognitive domain were correlated with higher (better) scores (for S5) or odds of a higher score (S3 and S4) on the CCTI standards.

Cognitive Predictors of Understanding (S5) Across Groups

Table 4 displays the results from the linear regression analyses predicting *understanding* (S5) for each group. All three models for S5 were significant. The control predictor model accounted for 48% of the variance in S5 performance, $F(4, 55) = 12.77, p < .001$. In the control model, the academic achievement and memory score composites were significantly related to S5 scores ($p = 0.002$ and 0.03 respectively). The mTBI model of S5 was also statistically significant ($R^2 = .62, F(4, 43) = 17.67, p < 0.001$). In the mTBI model, only the memory composite score predicted S5 scores ($p < 0.001$). The msevTBI model of *understanding* was also statistically significant ($R^2 = .76, F(4, 45) = 35.28, p < 0.001$). In this model, the academic achievement and memory composites predicted *understanding* scores ($p < 0.001$ and $p = 0.001$ respectively).

Cognitive Predictors of Reasoning (S4) Across Groups

The results for the ordinal regression models predicting *reasoning* are presented in Table 5. The control model of *reasoning* was not significant ($R^2 = .10, \chi^2(4) = 6.46, p = 0.168$). However, for the mTBI patients, the model for *reasoning* was significant ($R^2 = .34, \chi^2(4) = 19.61, p = 0.001$). Higher verbal memory scores were associated with increasing odds of higher *reasoning* scores ($OR = 1.31, 95\% CI = 1.05, 1.63, p = 0.018$). For msevTBI patients, the model for *reasoning* was also significant ($R^2 = .53, \chi^2(4) = 37.98, p < 0.001$); higher academic achievement scores were associated with increasing odds of higher *reasoning* scores ($OR = 1.29, 95\% CI = 1.04, 1.60, p = 0.018$).

Cognitive Predictors of Appreciation (S3) Across Groups

Results from the ordinal regression analyses for the *appreciation* standard are presented in Table 6. The model of *appreciation* for controls was not significant ($R^2 = .10, \chi^2(4) = 5.24, p = 0.264$). The model for the mTBI group was significant ($R^2 = .23, \chi^2(4) = 11.91, p = 0.018$); higher academic achievement scores were associated with increasing odds of higher *appreciation* scores ($OR = 1.41, 95\% CI = 1.08, 1.83, p = 0.011$). For msevTBI patients, the model of *appreciation* was also significant ($R^2 = .48, \chi^2(4) = 31.70, p < 0.001$); higher verbal fluency scores were associated with increasing odds of higher *appreciation* scores ($OR = 1.75, 95\% CI = 1.01, 3.03, p = 0.045$) and higher academic achievement scores were associated with increasing odds of higher *appreciation* scores ($OR = 1.29, 95\% CI = 1.03, 1.61, p = 0.025$) for msevTBI.

Secondary Analyses

We examined bivariate correlations between CCTI standard scores (S5-S3) and the cognitive domain scores separately for complicated and uncomplicated mild TBI cases. In general, correlations were similar but stronger for complicated mild TBI ($r=0.73$ to $r=0.80$) compared to the uncomplicated mild TBI ($r=0.27$ to $r=0.64$).

A score of 1.5 SD or greater below the control mean is often used as a cut score to determine impairment on cognitive and capacity assessments. None of the mean cognitive scores for the mild TBI group were 1.5 SD below the control group mean. However, when examined at the individual level, over half of the individuals within the mild TBI group not in PTA were impaired on at least one capacity standard using a score of 1.5 SD or below the control mean as a cutoff. For persons with moderate to severe TBI, approximately 77% of these individuals were impaired using the control mean cut-off.

In addition, we examined the possible relationship between effort and CCTI performance by conducting three additional regression analyses (one for each group) that included CVLT-II Forced Choice score and the four cognitive domain scores as predictors and S5 (*understanding*) as the dependent variable. The CVLT-II Forced Choice test was not significantly related to *understanding* scores for controls or mTBI ($p=0.160$ and $p=0.293$ respectively) but was for msevTBI ($p<0.001$). The same cognitive predictors were significant in the models for controls and mTBI. In the model for msevTBI, verbal memory remained a significant predictor ($p<0.001$) but academic achievement was just above the threshold ($p=0.051$). These results suggest that adding a motivation variable did not significantly alter the results from our analyses for *understanding*.

DISCUSSION

In the current study, we investigated cognitive models of medical decision-making capacity (MDC) for controls and adults with mild and moderate/severe TBI who were tested approximately one-month after injury using an established psychometric measure of MDC and a battery of neuropsychological tests. We examined *understanding* (S5), *reasoning* (S4), and *appreciation* (S3), which are the three most challenging and clinically relevant treatment consent standards described in the literature¹². The present study also expanded upon an earlier study of neurocognitive predictors of MDC in persons with moderate/severe TBI⁶ by including a group of mild TBI patients. Our results illustrate the importance of verbal memory and academic achievement skills in understanding and assessing treatment consent capacity in controls and persons with mild and moderate/severe TBI.

Understanding (S5) is the most stringent and cognitively complex consent ability^{7, 12, 22, 31-33}. Successful performance on this standard requires the ability to process, encode, consolidate, and recall new information relevant to the medical condition and associated symptoms, available treatment options, and the respective risks and benefits of each treatment option²⁰.

Verbal memory emerged as a significant predictor of *understanding* for all three groups. This is not surprising given the factual and memory intensive nature of the *understanding*

standard²¹, and the prevalence of short term memory impairment shortly after mild and moderate/severe TBI³⁴. The frontal and temporal lobe regions of the brain are most susceptible to damage in TBI and memory impairment is common following injury to these brain regions^{8, 35}. Even patients with mild TBI may experience difficulties in memory that can persist for a month or longer³⁶⁻³⁹, although full recovery is generally expected within three months after injury^{8, 40, 41}. The strong association between memory and *understanding* performance has also been documented in other patient populations, including individuals with mild cognitive impairment⁴² and brain cancer³³. Finally, as demonstrated in our study, the cognitive model for healthy adults also demonstrated the importance of verbal memory to normative performance on the *understanding* standard.

We also found that the academic achievement composite score predicted performance on *understanding* by both the control and moderate/severe TBI groups. In controls, the academic achievement composite score may represent a proxy for overall intellectual level⁴³, while in cognitively impaired TBI patients it may represent a form of cognitive reserve⁴⁴. As the *understanding* and other CCTI standards tap general conceptual knowledge as well as verbal memory²¹, it is not surprising that overall academic knowledge might predict performance on *understanding*. Put differently, a person's existing fund of academic knowledge appears to be a secondary predictor, after verbal memory, of performance on the *understanding* standard which has both conceptual as well as verbal memory demand characteristics⁴⁴.

Reasoning (S4) is a moderately stringent consent ability that requires a person to reason and compare relative risks and benefits of each treatment option, and then to use that information to make a treatment decision^{20, 22}. Cognitive abilities important for successful performance on this standard include memory of key factual information and executive functioning¹². For controls, the only unique cognitive predictor of *reasoning* was performance on semantic verbal fluency measures. Semantic verbal fluency measures speeded access and verbal expression of category specific semantic knowledge⁸, and has commonly emerged as a predictor of treatment consent abilities^{33,6}.

The relatively weaker control models for the *reasoning* and *appreciation* standards likely occurred because controls traditionally perform well on these simpler standards and the lack of heterogeneity in control performance on these standards makes it difficult to create strong predictor models. Therefore, the control models on S4 and S3 are limited by measurement issues.

For the mild TBI group, the verbal memory composite emerged as the only cognitive predictor of *reasoning*, although the executive function/processing speed composite approached significance ($p=0.054$). Memory is relevant to performance on *reasoning* because individuals who have difficulty recalling treatment information presented to them in the CCTI vignette have less information to consider when reasoning about the treatment options³³. Executive function is also relevant to *reasoning* because this standard requires the person to simultaneously and comparatively weigh risks and benefits of each treatment option in arriving at a decision.

In contrast, for the moderate/severe TBI group the academic skill composite was the only predictor of *reasoning* performance, although the verbal memory composite approached significance. During the early post acute injury phase, memory performance is almost uniformly poor for those with moderate-severe TBI, which undermines its predictive power. Academic skills are resistant to the effects of even severe TBI in many cases, meaning that this area of cognition can still differentiate TBI cases early in recovery. It is possible that people with higher levels of academic achievement can access overlearned paradigms of problem-solving that can be applied even in the presence of significant cognitive deficits.

Appreciation is a clinically-relevant consent ability that requires the individual to appreciate potential immediate and long-term personal consequences of a treatment decision¹². It requires personal judgment, memory of factual information, and executive abilities¹². Unlike the *understanding* and *reasoning* standards, the *appreciation* standard relies more on the person's past fund of personal and general knowledge and less on memory of newly presented factual information⁶. Empathy, emotional processing, planning, and foresight¹², which are abilities subserved by frontal lobe networks³⁵, are also related to successful performance on this standard.

Appreciation has typically been more difficult to model cognitively compared to the other consent standards because of the personal and projective aspects of this standard that are not captured with standard neuropsychological tests^{6,12,45}. The cognitive model of *appreciation* for controls was weak--all four cognitive domains together only explained 10% of the variance in control performance and none of the individual cognitive domains reached significance. Again, the lack of heterogeneity in the control group's scores on this standard likely resulted in our weak model.

For the mild TBI patients, the academic skills composite emerged as the only cognitive predictor of *appreciation*. However, this model only explained 23% of the variance in CCTI scores, again reflecting the difficulty modeling this consent ability with standard neuropsychological measures. In contrast, for moderate/severe TBI participants, the semantic fluency and academic skills composites were significant predictors of *appreciation* and together accounted for 48% of total variance.

The current study extended results from a previous study investigating cognitive predictors of MDC in a different sample of moderate/severe TBI patients⁶. In both studies, verbal memory was the primary predictor of *understanding*. However, some findings also differed between the two studies. For example, in the present study verbal fluency and academic skills predicted performance by moderate/severe TBI patients on *reasoning*, whereas in Dreer et al. short-term memory and attention were significant predictors⁶. Of course there are key methodological differences between the two studies that help explain occasional discrepancies. First, the present study included a much larger sample of TBI patients (N=104 versus N=34). Second, the data analytic approaches used in the two studies were different and likely contributed to different findings. In the present study, we used factor analysis to derive cognitive composite scores that were then used as independent variables in the regression analyses, whereas the prior study entered each cognitive test score separately into

the analyses. We also used simultaneous regression instead of stepwise regression and ordinal regression instead of linear regression for S3 and S4.

We found that a measure of TBI patients' test taking effort did not contribute to the results of this study. Results were essentially the same when the CVLT-II Forced Choice variable was added to the models, suggesting that test taking effort did not significantly impact our findings. Notably, base-rates of suboptimal effort in medical settings such as ours are generally reported to be 8% or less⁴⁶, which is much lower than the rate of 18%-64% of examinees being evaluated in the context of a forensic evaluation⁴⁷⁻⁴⁹.

Our study results have a number of scientific and clinical implications. First, memory appears to be an important baseline neurocognitive predictor of MDC regardless of consent ability and TBI injury severity. Interventions to support memory function may thus enhance the consent abilities of patients with TBI. For example, having disease and treatment-related information presented in written formats may help patients with TBI participate more fully in the treatment decision making process. Second, clinicians can use the overall study findings to better identify TBI patients at risk for diminished MDC. Specifically, clinicians may want to view impaired verbal memory and academic ability scores as potential "red flags" of diminished treatment consent capacity, and as a result more carefully examine MDC as needed in these patients.

There were several limitations to the study. First, individuals may respond differently to a hypothetical vignette than to real-life, personal medical situations. For example, real-life medical problems may trigger emotional aspects of MDC not captured by the CCTI vignettes. Second, while our study population was comparable to other TBI patient populations, participants in research studies may not completely reflect the general population. For example, we were unable to test some patients who were severely injured and consequently the findings may underestimate the level of MDC impairment in patients with severe TBI. Third, there were a few individuals in the moderate to severe TBI group who were not fully oriented at the time of this assessment. We decided not to exclude these individuals in this study because we wanted a representative sample of moderate to severe TBI cases. Fourth, we did not have sufficient sample size to create separate models of consent capacity for the complicated and uncomplicated mild TBI cases. Fifth, while our analytic approach had a number of strengths, our subgroup sample sizes were not large enough to permit separate factor analysis for each subgroup. Sixth, performance validity data was limited to the CVLT-II Forced Choice test; although the CVLT-II validity indicators have high specificity, there are other cognitive validity tests that have higher levels of sensitivity that may be useful to include in future investigations of MDC in TBI populations⁵⁰. In addition, the CCTI was administered and scored by only one person, so we could not examine inter-rater reliability in this study. Finally, cross-validation of the findings in other TBI samples would further establish external validity of the study findings.

Future directions include examining cognitive predictors of MDC for complicated and uncomplicated mild TBI, investigating non-cognitive predictors (i.e., psychiatric functioning, clinical factors, etc.) of MDC in TBI, and developing longitudinal cognitive models of MDC to examine predictors of capacity recovery in TBI. Finally, as noted there is

a need to investigate interventions to support or even improve MDC in patients with TBI. Studies might investigate which capacity intervention strategies are most effective for particular individuals, depending on their cognitive presentation and other clinical variables.

Acknowledgements

Study funding: Supported by the National Institute on Child Health and Human Development (1R01HD053074) (Marson, PI).

The authors thank the following contributors: Sandra Caldwell, MA (UAB Department of Physical Medicine and Rehabilitation, data collection); UAB Neuropsychology Laboratory Staff (data collection); Patrick Prichard, MD (UAB Department of Surgery, referring study participants); and Sarah Nafziger, MD (UAB Department of Emergency Medicine, referring study participants).

Statistical analyses were performed by Dr. Triebe, Department of Neurology, UAB, Birmingham, AL and Dr. Kennedy, Department of Medicine, UAB, Birmingham, AL.

REFERENCES

1. Fisk GD, Schneider JJ, Novack TA. Driving following traumatic brain injury: prevalence, exposure, advice and evaluations. *Brain Inj.* 1998; 12:683–695. [PubMed: 9724839]
2. Franulic A, Carbonell CG, Pinto P, Sepulveda I. Psychosocial adjustment and employment outcome 2, 5 and 10 years after TBI. *Brain Inj.* 2004; 18:119–129. [PubMed: 14660225]
3. Satz P, Forney DL, Zaucha K, et al. Depression, cognition, and functional correlates of recovery outcome after traumatic brain injury. *Brain Inj.* 1998; 12:537–553. [PubMed: 9653518]
4. Marson DC, Dreer LE, Krzywanski S, Huthwaite JS, Devivo MJ, Novack TA. Impairment and partial recovery of medical decision-making capacity in traumatic brain injury: a 6-month longitudinal study. *Arch Phys Med Rehabil.* 2005; 86:889–895. [PubMed: 15895333]
5. Dellasega C, Frank L, Smyer M. Medical decision-making in elderly hospitalized patients. *Journal of Ethics, Law, and Aging.* 1996; 2(2):65–74.
6. Dreer LE, De Vivo MJ, Novack TA, Krzywanski S, Marson DC. Cognitive predictors of medical decision-making capacity in traumatic brain injury. *Rehabilitation Psychology.* 2008; 53:486–497. [PubMed: 20686627]
7. Triebe KL, Martin RC, Novack TA, et al. Treatment consent capacity in patients with traumatic brain injury across a range of injury severity. *Neurology.* 2012; 78:1472–1478. [PubMed: 22496195]
8. Lezak, M.; Howieson, D.; Loring, D. *Neuropsychological Assessment.* 4th ed. Oxford University Press; New York: 2004.
9. Bowie CR, Leung WW, Reichenberg A, et al. Predicting schizophrenia patients' real-world behavior with specific neuropsychological and functional capacity measures. *Biol Psychiatry.* 2008; 63:505–511. [PubMed: 17662256]
10. Okonkwo OC, Wadley VG, Griffith HR, Ball K, Marson DC. Cognitive Correlates of Financial Abilities in Mild Cognitive Impairment. *J Am Geriatr Soc.* 2006; 54:1745–1750. [PubMed: 17087703]
11. Ortoleva C, Brugger C, Van der Linden M, Walder B. Prediction of driving capacity after traumatic brain injury: a systematic review. *J Head Trauma Rehabil.* 2012; 27:302–313. [PubMed: 21897289]
12. Marson DC, Chatterjee A, Ingram KK, Harrell LE. Toward a neurologic model of competency: Cognitive predictors of capacity to consent in Alzheimer's disease using three different legal standards. *Neurology.* 1996; 46:666–672. [PubMed: 8618664]
13. Gurrera RJ, Moye J, Karel MJ, Azar AR, Armesto JC. Cognitive performance predicts treatment decisional abilities in mild to moderate dementia. *Neurology.* 2006; 66:1367–1372. [PubMed: 16682669]

14. Kalmar K, Novack TA, Nakase-Richardson R, et al. Feasibility of a brief neuropsychologic test battery during acute inpatient rehabilitation after traumatic brain injury. *Arch Phys Med Rehabil*. 2008; 89:942–949. [PubMed: 18452744]
15. Dahmer E, Shilling M, Hamilton Bea. A model systems database for traumatic brain injury. *Journal of Head Trauma Rehabilitation*. 1993; 8:12–25.
16. Medicine ACoR. Definition of mild traumatic brain injury. *Journal of Head Trauma Rehabilitation*. 1993; 8:86–87.
17. Williams DH, Levin HS, Eisenberg HM. Mild head injury classification. *Neurosurgery*. 1990; 27:422–428. [PubMed: 2234336]
18. Russell W, Smith A. Posttraumatic amnesia in closed head injury. *Archives of Neurology*. 1961; 5:16–29.
19. McKinlay, W.; Watkins, A. Cognitive and behavioral effects of brain injury. In: Rosenthal, M.; Griffith, ER.; Kreutzer, J.; Pentland, B., editors. *Rehabilitation of the adult and child with traumatic brain injury*. F.A. Davis Co; Philadelphia: 1999. p. 74-86.
20. Marson DC, Ingram KK, Cody HA, Harrell LE. Assessing the competency of patients with Alzheimer's disease under different legal standards. A prototype instrument. *Arch Neurol*. 1995; 52:949–954. [PubMed: 7575221]
21. Dymek MP, Marson DC, Harrell L. Factor structure of capacity to consent to medical treatment in patients with Alzheimer's disease: An exploratory study. *Journal of Forensic Neuropsychology*. 1999; 1:27–48.
22. Appelbaum P, Grisso T. Assessing patients' capacities to consent to treatment. *N Engl J Med*. 1988; 319:1635–1638. [PubMed: 3200278]
23. Reitan, RM.; Wolfson, D. *The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation*. Neuropsychology Press; Tuscon, AZ: 1993.
24. Wechsler, D. *WAIS-III Wechsler Adult Intelligence Scale-Third Edition*. The Psychological Corporation; San Antonio, TX: 1997.
25. Corporation, TP. *Wechsler Test of Adult Reading*. Harcourt Assessment; San Antonio, TX: 2001.
26. Spreen, O.; Strauss, E. *A Compendium of Neuropsychological Tests*. Oxford University Press; New York: 1998.
27. Delis, D.; Kramer, J.; Kaplan, E.; Ober, B. *CVLT-II California Verbal Learning Test*. The Psychological Corporation; San Antonio, TX: 2000.
28. Wechsler, D. *WMS-III Wechsler Memory Scale-Third Edition*. The Psychological Corporation; San Antonio, TX: 1997.
29. Levin HS, O'Donnell VM, Grossman RG. The Galveston Orientation and Amnesia Test. A practical scale to assess cognition after head injury. *J Nerv Ment Dis*. 1979; 167:675–684. [PubMed: 501342]
30. Nagelkerke NJ. A note on a general definition of the coefficient of determination. *Biometrika*. 1991; 78:691–692.
31. Okonkwo O, Griffith HR, Belue K, et al. Medical decision-making capacity in patients with mild cognitive impairment. *Neurology*. 2007; 69:1528–1535. [PubMed: 17923615]
32. Martin RC, Okonkwo OC, Hill J, et al. Medical decision-making capacity in cognitively impaired Parkinson's disease patients without dementia. *Mov Disord*. 2008
33. Triebel KL, Martin RC, Nabors LB, Marson DC. Medical decision-making capacity in patients with malignant glioma. *Neurology*. 2009; 73:2086–2092. [PubMed: 20018637]
34. Sigurdardottir S, Andelic N, Wehling E, et al. Neuropsychological Functioning in a National Cohort of Severe Traumatic Brain Injury: Demographic and Acute Injury-Related Predictors. *J Head Trauma Rehabil*. 2014
35. Stuss DT. Traumatic brain injury: relation to executive dysfunction and the frontal lobes. *Curr Opin Neurol*. 2011; 24:584–589. [PubMed: 21968550]
36. Sterr A, Herron KA, Hayward C, Montaldi D. Are mild head injuries as mild as we think? Neurobehavioral concomitants of chronic post-concussion syndrome. *BMC Neurol*. 2006; 6:7. [PubMed: 16460567]

37. Vanderploeg RD, Curtiss G, Belanger HG. Long-term neuropsychological outcomes following mild traumatic brain injury. *J Int Neuropsychol Soc.* 2005; 11:228–236. [PubMed: 15892899]
38. Lee H, Wintermark M, Gean AD, Ghajar J, Manley GT, Mukherjee P. Focal lesions in acute mild traumatic brain injury and neurocognitive outcome: CT versus 3T MRI. *J Neurotrauma.* 2008; 25:1049–1056. [PubMed: 18707244]
39. Levin HS, Mattis S, Ruff RM, et al. Neurobehavioral outcome following minor head injury: a three-center study. *J Neurosurg.* 1987; 66:234–243. [PubMed: 3806205]
40. Rohling ML, Binder LM, Demakis GJ, Larrabee GJ, Ploetz DM, Langhinrichsen-Rohling J. A Meta-Analysis of Neuropsychological Outcome After Mild Traumatic Brain Injury: Re554 analyses and Reconsiderations of Binder et al. (1997), Frencham et al. (2005), and Pertab et al. (2009). *Clin Neuropsychol.* 25:608–623. [PubMed: 21512956]
41. Belanger HG, Vanderploeg RD. The neuropsychological impact of sports-related concussion: a meta-analysis. *J Int Neuropsychol Soc.* 2005; 11:345–357. [PubMed: 16209414]
42. Okonkwo OC, Griffith HR, Belue K, et al. Cognitive models of medical decision-making capacity in patients with mild cognitive impairment. *J Int Neuropsychol Soc.* 2008; 14:297–308. [PubMed: 18282327]
43. Green RE, Melo B, Christensen B, Ngo LA, Monette G, Bradbury C. Measuring premorbid IQ in traumatic brain injury: an examination of the validity of the Wechsler Test of Adult Reading (WTAR). *J Clin Exp Neuropsychol.* 2008; 30:163–172. [PubMed: 18213530]
44. Sumowski JF, Chiaravalloti N, Krch D, Paxton J, Deluca J. Education attenuates the negative impact of traumatic brain injury on cognitive status. *Arch Phys Med Rehabil.* 2013; 94:2562–2564. [PubMed: 23932968]
45. Dymek M, Atchison P, Harrell L, Marson D. Competency to consent to treatment in cognitively impaired patients with Parkinson's disease. *Neurology.* 2001; 56:17–24. [PubMed: 11148230]
46. Mittenberg W, Patton C, Canyock EM, Condit DC. Base rates of malingering and symptom exaggeration. *J Clin Exp Neuropsychol.* 2002; 24:1094–1102. [PubMed: 12650234]
47. Binder LM. Assessment of malingering after mild head trauma with the Portland Digit Recognition Test. *J Clin Exp Neuropsychol.* 1993; 15:170–182. [PubMed: 8491843]
48. Heaton RK, Smith HH Jr, Lehman RA, Vogt AT. Prospects for faking believable deficits on neuropsychological testing. *J Consult Clin Psychol.* 1978; 46:892–900. [PubMed: 701568]
49. Larrabee GJ. Detection of malingering using atypical performance patterns on standard neuropsychological tests. *Clin Neuropsychol.* 2003; 17:410–425. [PubMed: 14704892]
50. Root JC, Robbins RN, Chang L, Vang WG. Detection of inadequate effort on the California Verbal Learning Test-Second edition: forced choice recognition and critical item analysis. *J Int Neuropsychol Soc.* 2006; 12:688–696. [PubMed: 16961950]

Table 1

Demographic and Clinical Characteristics of Study Participants

	Range	controls n = 60	mild TBI n = 49	msev TBI n = 55	p [†]
Age	19-77	36.38 (12.48)	39.94 (15.10)	36.62 (15.23)	.367
Female, n (%)		24 (40.0)	22 (44.9)	11 (20.0)	.016
Race, n (%)					
African American		17 (28.3)	16 (32.7)	7 (12.7)	
Caucasian		43 (71.7)	32 (65.3)	47 (85.5)	.053 ^a
Hispanic		0	1 (2.0)	1 (1.8)	
Education	8-20	12.62 (1.33)	13.37 (2.40)	12.58 (2.48)	.105
GOAT score ^b	0-100	N/A	95.40 (5.86)	70.04 (32.42)	<.001
GCS score	0-15	N/A	14.46 (1.50)	5.76 (2.98)	<.001

Except for gender and race, values are mean (SD).

[†] p value for omnibus test of group differences. TBI = mild traumatic brain injury; msev = moderate to severe; GOAT = Galveston Orientation and Amnesia Test; GCS = Glasgow Coma Scale.

^a Comparison between Caucasian vs non-Caucasian groups.

^b = GOAT scores available for 52 msevTBI patients.

Table 2

Group Comparisons on CCTI Consent Standards (S)

Measures	Range	controls n = 60	mild TBI n = 49	msevTBI n = 55	p [†]	post hoc
S1, expressing choice	0 - 4	3.98 (0.13)	3.90 (0.37)	3.46 (1.34)	.001	C, mild > msev
[S2], reasonable choice, n (%)						
Yes	0 - 1	58 (96.7)	48 (98.0)	47 (85.5)	.015	C, mild > msev
No		2 (3.3)	1 (2.0)	8 (14.5)		
S3, appreciation	0 - 8	7.58 (0.79)	6.69 (1.52)	4.93 (2.80)	<.001	C > mild > msev
S4, reasoning	0 - 12	8.85 (2.46)	7.59 (3.07)	4.55 (3.61)	<.001	C, mild> msev
S5, understanding	0 - 79	63.73 (8.90)	53.18 (14.62)	30.60 (20.74)	<.001	C > mild > msev

Except for [S2], values are mean (SD).

[†]p value for ANOVA omnibus test of group differences (S1, S3 – S5), or Pearson's chi square test [S2].

Post hoc comparisons using Bonferroni multiple comparisons test (S3-S5) or pairwise χ^2 analyses [S2] (significant differences at .05).

CCTI = Capacity to Consent to Treatment Instrument; S = standard; C = controls; TBI = traumatic brain injury; msevTBI = moderate to severe traumatic brain injury.

C > mild > msev = control mean greater than mild TBI and msevTBI means, and mild TBI mean greater than msevTBI mean; C, mild > msev = control and mild TBI means greater than msevTBI mean.

Table 3

Group Comparisons on Selected Neuropsychological Measures

Measures	controls n = 60	mild TBI n = 49	msev TBI n = 55	F	df	p [†]	Post hoc comparisons
Processing Speed/Executive Function Composite	10.23 (1.98)	7.98 (3.12)	3.55 (2.46)	100.76	159	<.001	C > mild > msev
Verbal Fluency Composite	9.44 (2.27)	7.42 (2.81)	4.04 (1.84)	74.81	156	<.001	C > mild > msev
Verbal Memory Composites	9.51 (2.52)	7.77 (3.12)	3.30 (2.53)	77.91	160	<.001	C > mild > msev
Academic Abilities	9.91 (2.34)	8.82 (2.77)	6.56 (3.48)	19.61	160	<.001	C > mild > msev

Note. Values reported are scaled scores (mean of 10, SD of 3) based on normative data. Values are mean (SD).

[†] p value for *F* test of group differences. Post hoc comparisons using Bonferroni multiple comparisons test.

TBI = Traumatic Brain Injury; msev = moderate/severe;

Table 4
Neuropsychological Predictors of CCTI Performance on Understanding (S5) in Controls and Patients with Traumatic Brain Injury

Estimates are the effect of a 1-unit increase in the factor on S5 scores.

Factor	Controls, n = 60				Mild TBI, n = 49				Mod/Sev TBI, n = 55			
	Estimate	Standard Error	p-value	R ²	Estimate	Standard Error	p-value	R ²	Estimate	Standard Error	p-value	R ²
Verbal Fluency	.099	.415	.813	.482	.567	.733	.444	0.622	.977	1.412	.492	0.758
Academic	1.617	.500	.002		1.140	.634	.079		2.835	.631	<.001	
Executive / Processing Speed	.643	.518	.220		.356	.634	.578		-.071	.821	.932	
Memory	.924	.417	.031		2.464	.580	<.001		3.499	1.018	.001	

Table 5
Neuropsychological Predictors of CCTI Performance on Reasoning (S4) in Controls and Patients with Traumatic Brain Injury
 Odds ratios are the odds of *higher* scores on S4 for a 1-unit increase in the factor. The Nagelkerke R^2 was used as a measure of the model fit.

Factor	Controls, n = 60			Mild TBI, n = 49			Mod/Sev TBI, n = 55		
	Odds Ratio (95% CI)	p-value	R ²	Odds Ratio (95% CI)	p-value	R ²	Odds Ratio (95% CI)	p-value	R ²
Verbal Fluency	0.799 (0.640, 0.997)	.047	.104	0.976 (0.748, 1.275)	.860	.339	1.307 (0.827, 2.069)	.252	.529
Academic	1.060 (0.816, 1.376)	.662		0.949 (0.754, 1.197)	.662		1.289 (1.041, 1.598)	.020	
Executive / Processing Speed	1.133 (0.863, 1.486)	.368		1.264 (0.996, 1.605)	.054		0.975 (0.748, 1.270)	.851	
Memory	1.170 (0.938, 1.458)	.164		1.309 (1.048, 1.634)	.018		1.387 (0.988, 1.946)	.059	

Table 6
Neuropsychological Predictors of CCTI Performance on Appreciation (S3) in Controls and Patients with Traumatic Brain Injury

Odds ratios are the odds of *higher* scores on S3 for a 1-unit increase in the factor. The Nagelkerke R^2 was used as a measure of the model fit.

Factor	Controls, n = 60			Mild TBI, n = 49			Mod/Sev TBI, n = 55		
	Odds Ratio (95% CI)	p-value	R ²	Odds Ratio (95% CI)	p-value	R ²	Odds Ratio (95% CI)	p-value	R ²
Verbal Fluency	1.192 (0.882, 1.614)	.253	.104	0.827 (0.614, 1.114)	.211	.231	1.754 (1.013, 3.034)	.045	.479
Academic	0.998 (0.721, 1.380)	.988		1.408 (1.082, 1.829)	.011		1.289 (1.031, 1.611)	.025	
Executive / Processing Speed	0.913 (0.638, 1.306)	.618		1.085 (0.841, 1.399)	.530		1.083 (0.804, 1.459)	.599	
Memory	1.235 (0.910, 1.674)	.175		1.088 (0.866, 1.366)	.471		0.950 (0.659, 1.369)	.782	