Participation in dementia research: rates and correlates of capacity to give informed consent

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ABSTRACT

Background: Many people participating in dementia research may lack capacity to give informed consent and the relationship between cognitive function and capacity remains unclear. Recent changes in the law reinforce the need for robust and reproducible methods of assessing capacity when recruiting people for research.

Aims: To identify numbers of capacitous participants in a pragmatic randomised trial of dementia treatment; to assess characteristics associated with capacity; to describe a legally acceptable consent process for research.

Methods: As part of a pragmatic randomised controlled trial of Ginkgo biloba for mild-moderate dementia, we used a consenting algorithm that met the requirements of existing case law and the exigencies of the new Mental Capacity Act. We decided who had capacity to give informed consent for participation in the trial using this algorithm and sought predictors of capacity.

Results: Most participants (76%) with mild-moderate dementia in this trial were unable to give informed consent according to the legal criteria. When adjusted for confounding, the Mini Mental State examination did not predict the presence of capacity.

Conclusion: Cognitive testing alone is insufficient to assess the presence of capacity. Researchers and clinicians need to be aware of the challenging processes regarding capacity assessment. We outline a procedure which we believe meets the ethical and legal requirements.

The Mental Capacity Act for England and Wales includes a legal framework for individuals lacking capacity who participate in research.[1] The Act came into force in April 2007 as regards Independent Mental Capacity Advocates and as regards the remainder of the Act in October 2007. This Act codifies established common law principles of consent and introduces a number of new principles. Whilst the common law legal test for capacity is a three stage test (see later for detail) the new test is a two step, four stage process.

A patient will be deemed to lack capacity if they have an impairment of, or a disturbance in their mind or brain which renders them unable to make a choice. They are unable to make a choice if they cannot retain or understand the treatment information, weigh the information up to make a decision or communicate their wishes. Importantly, the new act does not give precise guidance on practical assessment of capacity although the newly published Code of Practice does to an extent (chapter 4).

Previous studies have cast doubt on clinicians' and researchers' knowledge of the concept of capacity and its assessment, and in our experience as educators many health professionals, including researchers, are uncertain about what constitutes informed consent and clinicians rarely have sufficient knowledge of the legal test for capacity to satisfy the courts.[2]

Many individuals with dementia who participate in research are likely to lack capacity, and there has been insufficient research on the relationship between ability measures and cognitive capacity.[3 4] Greater respect for autonomy and increasing risk of civil and criminal litigation around consent issues may weaken the current practice of recruiting non-capacitous individuals in research, make carers less likely to agree to participation, and ultimately deter research in dementia.[5]

Brief cognitive assessments, such as the Mini Mental State Examination (MMSE)[6] have been suggested as a marker of capacity[7 8] and are suggested as part of the capacity assessment[9] although their utility in assessing capacity remains unclear.[10] Most studies on this issue have evaluated individuals specifically recruited for consent research, which may not reflect the characteristics of individuals participating in real pragmatic treatment trials.

The aims of this study were:

1. to assess the proportion of people taking part in a randomised controlled trial of dementia treatment who were deemed to have capacity to consent to participate in research.
2. Using current English common law (which reflects emerging statute law) as a framework for obtaining consent, we describe an operationalised approach to assessing capacity in a research setting
3. To identify those variables associated with the presence of capacity.

METHODS

The study we report here involves analysis of participants in a randomised, double-blind, placebo-controlled, parallel group 6-month trial of a standardised extract of Ginkgo biloba leaf in mild-moderate dementia. This trial was approved by South West Multi-Centre Research Ethics Committee (ref: MREC/02/6/35) and was registered with Current Controlled Trials (ISRCTN45577048). Participants were eligible for the clinical trial if they met DSM-IV criteria for dementia, had a MMSE score of 12–26, did not have a clotting abnormality and had a carer who was willing to take part. The primary outcome measure was the cognitive part of the Alzheimer Disease Assessment Scale (ADAS-cog) where individuals score 0–70: a higher score

indicating worse cognitive functioning.[11] Participants lived in the community in and around the greater London area and were recruited via their doctor in primary and secondary care settings. Potential participants were provided with written information about the study before being visited by a researcher who provided further verbal information and answered any questions. The researcher then assessed capacity according to a protocol based on UK case law (see below), and obtained consent where appropriate.

The definition of capacity derives from the case of Re C. (1997).[12] In that case, the High Court held that an adult has capacity if he can:

a. understand and retain the treatment information
b. believe it; and
c. weigh it in the balance to arrive at a choice

Additionally the patient must be able to communicate his or her choice.

Stage (b) often leads to confusion; this part of the capacity assessment requires the patient to be orientated in reality as far as the information relating to the *decision in question* is concerned. Although the Mental Capacity Act 2005 omits the "belief" requirement from the new capacity test, it is likely that the courts will interpret understanding to include a requirement for an orientation in reality. Although these principles of obtaining consent for treatment apply equally to research, there are important differences in the research setting. In a therapeutic clinical trial, by definition, there is uncertainty concerning the benefits and risks of the treatment, and therefore greater scope for rational disbelief and weighing of possible risk and benefit.

We designed a consenting procedure based on the principles outlined above, to assess whether the individual meets criteria for capacity to provide informed consent for research. This included:

1. providing sufficiently detailed, salient written and verbal information to potential participants in a form they should be able to understand, including (a) the objectives of the trial, (b) potential risks and inconveniences of participation, (c) the product (Ginkgo) being tested and the possibility of receiving an inert placebo, (d) the concept of randomisation, (e) length of the trial and outcomes measured (f) the opportunity to withdraw at any time. Depending on the ability of the participant to assimilate information, the researcher repeated this information as necessary and at times requested the participant's carer to help impart information.
2. allowing sufficient time for the individual to understand and retain this information. This was assessed by the researcher judging, after providing the information in various ways, whether the participant was likely to be able to meet these criteria. If the researcher felt this was unlikely the participant was deemed to lack capacity
3. testing whether the potential participant has retained salient information, for example, by asking them to repeat relevant information and demonstrate understanding of this.
4. ensuring the potential participant was able to weigh this information in the balance and decide whether or not they wanted to participate, without coercion.

Researchers made a judgement about the potential participants' ability to acquit themselves at each stage of the consent process. If a participant fulfilled all four stages he/she was deemed to have met the criteria for informed consent. If a potential participant failed at any stage, we judged them to lack ability to give informed consent. Under such circumstances, an individual could still participate provided they indicated their assent (ie, agreed take part), and a relative or carer also agreed.

After recruiting a participant, we collected baseline demographic and clinical data including data on age, gender, ethnicity, years of education, type of dementia (defined by DSM-IV), carer-reported chronicity of dementia, MMSE score and ADAS-cog score. MMSE scores were dichotomised around the conventional cut-point of 24.

Associations between capacity (consent versus assent) and the following predictors were investigated: clinical diagnosis (Alzheimer disease versus vascular dementia); gender; ethnic origin (other versus white); MMSE score ($>=24$ versus <24); age (years); length of education (years); duration of dementia (months) and ADAS-Cog score. Single variable analysis was undertaken by fitting separate logistic regression models for each of the predictors. Odds ratios with 95% confidence intervals were obtained, along with p-values using the likelihood ratio chi-square test. Multivariable logistic regression was then undertaken. All the above variables were entered into a single model. The significance of each variable in the model was then assessed using the likelihood ratio chi-square test. The least significant term was removed and the model re-fitted. This process was iterated to identify which of the above variables were significantly independently associated with the presence of capacity.

RESULTS

Our sample had a mean age of 79 (range 57 to 96, SD 7.6), 106 (60% were female). The mean length of education was 11 years (SD 2.7). Median duration of dementia as reported by the carer was 36 months (inter-quartile range (IQR) 24 to 60); 148 (84%) had DSM-IV diagnosis Alzheimer disease and 28 (16%) had vascular dementia. Median baseline MMSE score was 22 (IQR 18 to 25) and median ADAS-Cog score was 21 (IQR 15 to 29).

Forty-two (24%) of the 176 participants were assessed as able to give informed consent when they started the trial. One participant has incomplete data: the following results are based on the remaining 175. Thirteen people who scored 26 on the MMSE were found unable to give informed consent, whereas two people who did have capacity to consent scored only 19 on the MMSE.

On single variable analysis using a conventional significance level of 5%, the presence of capacity was statistically significantly associated with: a diagnosis of Alzheimer's disease (OR = 0.342, 95% CI (0.146, 0.799), p = 0.015); age (OR = 0.916, 95% CI (0.872, 0.962), $p<0.001$); ADAS-Cog score (OR = 0.830, 95% CI (0.771, 0.893), $p<0.001$) and an MMSE score of 24 and above (OR = 6.271, 95% CI (2.920, 13.471), $p<0.001$). From the multi-variable logistic regression, with 5% significance level, the only variables independently significantly associated with decreased capacity was ADAS-Cog score and age (see table 1).

DISCUSSION

The granting of Royal Assent to the Mental Capacity Act (2005), implementation of the European Clinical Trials directive and recent case law have brought issues of capacity in research into sharper focus. Most people in our dementia trial were not able to provide informed consent using assessments based on current law.

As individuals who refused to take part were not assessed for capacity, we are unable to say how many of them would have been able to give their informed consent. This highlights an important distinction between clinical practice, where patients

Table 1 Showing differences between those participants with capacity to give informed consent and those who agreed to participate but lacked capacity (assent)

Summary for categorical variables		Consent Number (%)	Assent Number (%)	Total	Odds of consent of baseline (95% CI)	p Value
Diagnosis	Vascular dementia	12 (42.9%)	16 (57.1%)	28	Baseline	0.015
	Alzheimer's disease	30 (20.4%)	117 (79.6%)	147	0.342 (0.146, 0.799)	
Gender	Male	22 (31.4%)	48 (68.6%)	70	Baseline	0.062
	Female	20 (19.0%)	85 (21%)	105	0.513 (0.255, 1.035)	
MMSE score	12–23	13 (11.6%)	99 (88.4%)	112	Baseline	<0.001
	24–26	28 (45.2%)	34 (54.8%)	62	6.271 (2.920, 13.471)	
	Maximum	26	26			
	Minimum	19	12			
Summary for continuous variables		**Consent**	**Assent**	**Total**	**Odds ratio (95% CI)**	**p Value**
Age (years)	Mean (SD)	75.9 (7.0)	80.7 (7.3)	79.5 (7.6)	0.916 (0.872, 0.962)	<0.001
	Minimum	57	57	57		
	Maximum	89	96	96		
Education (years)	Mean (SD)	11.5 (3.4)	10.6 (2.5)	10.8 (2.7)	1.116 (0.991, 1.257)	0.074
	Minimum	6	7	6		
	Maximum	22	23	23		
Duration of dementia (months)	Median	30.0	42.0	36.0	0.990 (0.977, 1.002)	0.077
	Minimum	6	4	4		
	Lower quartile	17.5	24.0	24.0		
	Upper quartile	48.0	60.0	60.0		
	Maximum	156	216	216		
ADAS-COG (score)*	Median	15.0)	24.0	21.0	0.830 (0.771,0.893)	<0.001
	Minimum	6.0	8.0	6.0		
	Lower quartile	11.7	17.5	15.0		
	Upper quartile	17.0	32.5	29.0		
	Maximum	35.0	56.0	56.0		

Normally distributed data (mean and sd) and non-normal data (median and interquartile range) showing results of single variable comparisons of binary variables associated with presence/absence of capacity to consent to research. *Only ADAS-Cog score and age found to be independently associated with capacity using all the above variables in a multivariable logistic regression.

who lack capacity and refuse treatment may nevertheless be treated under common law, and research, where non-capacitous refusers are invariably excluded from participation. Research may be undertaken with incapacitious participants who nevertheless appear to agree to participation, but is only permissible if there is some potential direct or indirect benefit to the patient and the research cannot be carried out on patients who have capacity.

In some countries—for example, Australia and the USA—mechanisms exist for proxy consent in research.[13] Under the new Act if a patient has appointed a Lasting Power of Attorney or has a Deputy then such people may sign a research consent form on the patient's behalf. However the Act is silent as to whether a person who is purely being consulted within the meaning of section 32 needs to also sign the form. This section imposes a duty to consult with carers and other relevant people before involving an incapacitious patient in research and, if the carer believes the patient would have refused, the patient should not be involved.

Although there was a significant relationship between MMSE scores and capacity on univariate analysis, the significance of this association disappears after controlling for confounders (such as age and diagnosis), and the correlation was far from absolute: some individuals scoring 26 did not have capacity while two individuals who scored 19 did. The use of cognitive measures as a criterion when assessing capacity risks disenfranchising capacitous individuals with low scores, and erroneously recruiting non-capacitous individuals. Although it is useful to assess the degree of cognitive impairment as part of the overall clinical picture when judging capacity, we believe that the use of cognitive measures as a proxy for judging capacity is limited. For example, the nuances of appreciation required to understand the concept of randomisation would not be tested using standard measures of cognition. Attempts have been made to develop capacity scales for research and treatment.[8 14] Inevitably, these would need to be adjusted for each study as the nature, risks and benefits for any study are unique. Furthermore, the absolute gold standard (at least in legal forums) is the judgement of capacity at the time of assessment using the legal principles outlined here, rather than questionnaires or other measures.

This study has some limitations. Capacity was assessed by a single, albeit trained, researcher and there was no external assessment to evaluate the validity of the consent process. However, the procedure used meets the legal standard and is likely to be acceptable in a court. Assessing the validity and reliability of the consent process described here would require different methodology and would not be feasible in the setting of a clinical trial. Another limitation, inherent in all methods of assessing capacity is whether it is possible to truly demonstrate whether the individual giving consent really understands and believes the information provided to them. We believe we allowed individuals sufficient time to assimilate information if they were capable of doing so. However, the amount of time required and the assessment of understanding is always a matter of judgement which cannot easily be operationalised. Assessing this is de facto arbitrary and can only really be tested by proxy, for example by discussion with the individual. Our methods are congruent with expectations in English courts in this regard.

Capacity varies both according to the complexity of the information to be understood and over time. There is probably greater uncertainty in research than in clinical settings, and for this reason the information required to be understood by the participant is likely to be more complex. Patients with dementia

may experience lucid intervals and a person may have capacity to consent to a form of treatment or procedure when, for instance, medical advice is unequivocal, but lack the capacity to make more complex decisions. It is incumbent on researchers to assess, and reassess capacity at each stage of research and for each procedure, and on research ethics committees and sponsors to ensure that this is done. The issues and principles identified in this paper would apply equally in a clinical arena, and previous research has identified a significant need for education of clinicians as well as researchers about capacity assessment.[2]

There may never be a definitive indicator of capacity. There is an inevitable element of subjectivity and clinicians and researchers will have to adapt their approach each time they assess a patient, taking into account the unique intelligence and communication skills of the individual before them. But they need to bear in mind the four key elements to assessing capacity: providing salient, comprehensible information; allowing time to understand and retain it; testing retention and belief; and assessing ability to weigh the information. Only the first of these is usually scrutinised by research ethics committees. In any event, it is vital that a clinician or researcher records not only the finding of capacity or incapacity but also the basis for the finding.

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