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Cognitive Functioning in Complicated Grief

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Abstract

Complicated grief (CG) is increasingly recognized as a debilitating outcome of bereavement. Given the intensity of the stressor, its chronicity, and its association with depression, it is important to know the impact CG may have on cognitive functioning. This exploratory and descriptive study examined global and domain-specific cognitive functioning in a help-seeking sample of individuals with CG (n=335) compared to a separately ascertained control sample (n=250). Cognitive functioning was assessed using the Montreal Cognitive Assessment (MoCA). Controlling for age, sex and education effects, CG participants had lower total MoCA, visuospatial and attention scores relative to control participants. The two groups did not differ significantly in the domains of executive function, language, memory or orientation. Age, sex, and education accounted for much of the variance in MoCA scores, while CG severity and chronicity accounted for a very small percentage of MoCA score variance. Major depression was not a significant predictor of MoCA scores. This study is consistent with previous work demonstrating lower attention and global cognitive performance in individuals with CG compared to control participants. This study newly identifies the visuospatial domain as a target for future studies investigating cognitive functioning in CG.

Introduction

Bereavement and the experience of grief are among life's most stressful events¹. Despite this stress, most individuals come to accept the finality of the death, its consequences, redefine their life goals and adjust to life without their loved one². However, for some, the acute grief process is stalled, leading to prolonged or complicated grief (CG). Symptoms of CG include intense sorrow, guilt, deep yearning for the deceased; preoccupation for the loved one or events surrounding the death; avoidance of reminders of the loss; bitterness, and difficulty trusting or caring for others^{3,4}.

Much evidence suggests that CG is a disorder distinct from conditions with overlapping symptomatology such as post traumatic stress disorder (PTSD) and depression^{5,6,7}. The American Psychiatric Association (APA) has included provisional criteria for the diagnosis

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of CG, designated “Persistent Complex Bereavement Disorder (PCBD), in section III of the DSM-5⁸.

Early studies have estimated the prevalence of CG to be 4–5% in the general population and 7–5% among bereaved individuals^{9,10}. The impact of CG on society and among bereaved individuals and their families is profound. Comorbidity with other psychiatric disorders such as depression tends to be significantly higher in individuals with CG compared to the general public. In a clinical study, a concurrent major depressive disorder (MDD) was present in 55% of individuals with CG¹¹. Given the intensity of the stressor and its association with depression, understanding the impact CG may have on cognition is important.

Previous studies have suggested that individuals with CG have greater neurocognitive deficits compared to both normally bereaved and non-bereaved control participants in community based samples^{12 13}. This study represents an exploratory and descriptive analysis. It builds on previous work by exploring the association of CG with cognitive function in a sample of participants in a multisite NIMH-sponsored clinical trial researching treatment for CG and describing what may be an associated feature of the disorder. We examined cognitive functioning both globally and across six neurocognitive domains. After accounting for variables associated with cognitive functioning such as age, education, and depression, we examined whether variance in cognitive dysfunction might be explained by the presence of, severity or chronicity of CG symptoms.

Methods

1. Primary study description

We used data from a multicenter, double blind, placebo-controlled intervention trial entitled “Optimizing Treatment for Complicated Grief” (Healing Emotions After Loss: **HEAL**). The study began in March 2010 and is an ongoing NIMH sponsored clinical trial investigating the effects of citalopram versus placebo, with and without complicated grief therapy (CGT) [[ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01179568) Identifier: NCT01179568]. The study is being conducted in Boston New York, Pittsburgh and San Diego. Participants were recruited through a variety of methods including referrals from health care professionals and facilities (21%), non-health care personnel or agencies (6%), print media (20%), and broadcast or internet media (41%). The analyses reported here used pretreatment data from all randomized individuals as of January 16, 2014.

Inclusion criteria required an Inventory of Complicated Grief (ICG)¹⁴ score of 30 or greater at least 6 months after the death of a loved one, CG confirmed as present and the primary problem on clinical interview, and English fluency. Individuals were excluded from the study for any of the following reasons: substance abuse or dependence within the past 6 months, history of a psychotic disorder, current psychotherapy or treatment with an antidepressant, a Montreal Cognitive Assessment (MoCA) score <21, active homicidal ideation or when considered at immediate risk for suicide.

2. Archival control group

Our control sample was taken from previously published data comparing performance on the MoCA and the Mini-Mental Status Examination (MMSE) in cognitively normal individuals¹⁵. Most participants were from a convenience sample consisting of spouses and friends of patients seen at the University of California, San Diego (UCSD) Huntington's disease Research Center and UCSD Shiley-Marcos Alzheimer's Disease Research Center. Participants were excluded if they reported a lifetime history of neurologic or psychiatric disorders, or the use of psychoactive substances or medications.

3. Measures

Complicated grief was measured using the ICG¹⁶. The ICG is a 19-item self-report questionnaire reflecting the core emotional, behavioral and psychological symptoms of CG. Each of the 19-items are given a severity score between 0 (never) and 4 (always). Possible total scores range from 0–76. All study participants scored 30 or greater on the ICG.¹⁷ Cognitive function was measured using the Montreal Cognitive Assessment (MoCA) a screening tool for mild cognitive impairment and dementia¹⁸. The range of possible scores was 21–30. The lower limit was set at 21 in the HEAL study in order to rule-out individuals with probable dementia. Therefore, we used only control participants who earned scores in the same range (21–30). In each participant, we assessed the six neurocognitive domains (visuospatial ability, executive functioning, language, delayed memory, attention and orientation) represented in the MoCA. Executive function was measured by the sum of a participant's scores in the trail making, fluency, and abstraction tasks. Language was measured by the sum of the repetition and naming tasks. The visuospatial domain was measured using the sum of the cube and clock drawing tasks. Scores on the delayed recall task were used to assess delayed memory. Attention/ concentration and orientation were assessed as given on the MoCA.

Current mood disorder was evaluated using the Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition (SCID)¹⁹.

Depression severity was assessed using the 16-item version of the Quick Inventory of depressive symptomatology self-report (QIDS-SR-16)²⁰. Possible total scores range from 0–27.

Medical morbidity and burden were assessed using the Cumulative Illness Rating Scale (CIRS)²¹ a comprehensive review of medical problems by 14 organ systems. The CIRS rates each organ system between 0 (no problem) and 4 (end organ failure/ severe functional impairment). The organ category “,other” was omitted in the primary (HEAL) study, therefore, severity ratings were assessed for 13 organ systems. Possible total scores range from 0–52. For the purposes of this analysis, the categories of vascular and heart disease (combined mean) and neurological disease were reported as these organ systems are most likely to impact cognition. Total score included all 13 organ systems. Number of organ systems affected indicates the number of organ system categories (range 0–13) rated with a severity greater than zero.

4. CG Consort chart description

One-thousand-nine-hundred-thirty-nine individuals were screened over the telephone using the brief grief questionnaire (BGQ)²². The BGQ is a five-item self-administered screening tool that evaluates some of the core CG symptoms. Responses were rated as 0, not at all; 1, somewhat; or 2, a lot. A score of 5 or greater raises clinical suspicion for CG²³. Of the 1939 individuals screened, 1420 received a score of 5 or greater on the BGQ and were invited for a face-to-face baseline clinical assessment; 1,072 were excluded for various reasons (see fig. 1 for details). 348 participants were randomized to treatment, 13 had incomplete or missing MoCA data and were excluded from the analysis. The remaining 335 participants comprised the CG study group used in our analysis. All data for this analysis were collected at the baseline clinical assessment. The same procedures regarding recruitment and assessments described above were used at all four clinical sites.

5. Statistical analysis

Descriptive statistics were generated to characterize the CG and control participants on demographic measures (age, gender, race and education). Differences between groups were tested using t-tests for continuous variables and Chi-square test or Fisher Exact test for categorical variables. Descriptive statistics also further characterized the CG participants on the clinical measures of complicated grief, depression and medical burden.

Total MoCA scores were calculated using the sum of the items. Because persons with 12 years of education or less tend to have worse MoCA performance, one point is usually added to the total score to correct for educational effects²⁴. For the purposes of our study an extra point was not added since level of education was used as covariate in our analyses. Analysis of covariance (ANCOVA) tested for group differences controlling for age, gender and education. Analyses were repeated in participants ≥ 60 years of age since older adults are often most sensitive to cognitive changes. An additional sub analysis was done with CG participants alone since some CG participants MoCA's were administered at baseline before discontinuing any current antidepressant use. The ANCOVA was repeated in CG participants alone to test the possible effect of antidepressant medication.

Given the limited possible score range of each MoCA domain; an ordered logistic regression was used to test whether CG and control participants differed in any of the MoCA domains. These analyses controlled for age, gender and education. Bar charts show distribution of scores used in the analyses.

Multiple linear regression models were used in the CG sample alone in order to examine the effects of depression and CG severity on global MoCA scores after controlling for known effects of demographic variables.

6. Informed consent

“HEAL” was overseen by a Data and Safety Monitoring Board and reviewed by Institutional review boards at each of the participating study sites. Participants in both sample groups (CG and control) gave written informed consent.

Results

Participant descriptors

CG participants included both men and women between the ages of 19–89. CG participants had a mean (SD) age of 53($\pm$ 15 years), were predominantly female (80%) and white (85%).. The control sample was half female. Years of formal aging were comparable in the two groups (Table 1)

Regarding clinical characteristics (Table 2) the mean score on the Inventory of Complicated Grief (ICG) was 43 ($\pm$ 9). The mean time since the death of a loved one was 5 ($\pm$ 7) years with median time of 2 years. 67% (n= 223/335) of CG participants had a diagnosis of current MDD. The mean total QIDS score was 13 ($\pm$ 4) indicating a mild to moderate level of depression. The mean total CIRS score for medical comorbidity was 6 ($\pm$ 4), with the mean number of organ systems affected, 5 ($\pm$ 3).

Global cognition

The mean (SD) MoCA score in CG was 26.8 ($\pm$ 2.2) compared with 27.1 ($\pm$ 2.2) in control participants. The median MoCA score was 27 in CG and 28 in control participants (Table 3.).

Results of ANCOVA showed that an increased age was associated with decrease in MoCA score ($F(1,578)=57.42$, $p<0.0001$, explained variance=9.3%). Being female and having more education were both associated with higher scores ($F(1,578)=5.39$, $p=0.02$, explained variance=0.3) and ($F(3,578)=9.78$, $p<0.0001$, explained variance=4.1%) respectively. Controlling for age, sex and education effects, control participants had higher MoCA scores than CG participants ($F(1,578)=9.11$, $p=0.003$, explained variance=1.3%, least square means: CG = 26.5 vs. CTRL = 27.1). Age, sex, education and group membership (CG vs. Control) explained 15% variance in MoCA total scores, while group membership alone explained 1.3% of variance above and beyond what was explained by demographic measures. In a sub-analyses examining only participants ≥ 60 years of age, group was no longer significant ($F(1,210)=3.12$, $p=0.08$).

Total MOCA scores did not differ in sub-analyses comparing CG participants on psychotropic medications vs. CG participants not on psychotropic medications ($F(6,328)=0.01$, $p=0.91$, LSMEANS adjusting for age, gender and education: 26.61 vs. 26.58 respectively).

Among potential participants with an ICG score of 30 or higher and at least 6 months elapsed since the death of a loved one, none had MOCA scores less than 21.

Domain specific cognition

Table 3 displays the mean, median and range of both CG and control participants for each of the six neurocognitive domains. Results of the ordered logistic regression show that increased age was significantly associated with lower scores in all domains except attention and orientation (at $p<0.05$). Females had higher MoCA scores than males in the language and memory domains. Higher education was associated with higher scores in the executive,

language and attention domains. Controlling for age, sex and education effects, control participants were more likely to have higher visuospatial and attention scores than CG participants (odds ratios [95%CI]: 1.92 [1.34–2.75] and 1.68 [1.12–2.51] respectively.) The two groups did not differ significantly in the domains of executive function, language, memory or orientation.

Cognitive changes attributed to depression and severity of CG

In the multiple linear regression models using only the CG sample, age and education, but not gender, were significant predictors of total MoCA score. Increased age was associated with lower MoCA scores, and higher levels of education, with higher MoCA scores. There was a site difference such that the NY site had lower MoCA scores than the other sites. We controlled for this site related difference in the analyses. The demographic variables explained 12.1% of variance seen in total MoCA scores. Current MDD diagnosis was not a significant predictor and neither was time since loss (explained variance <0.01%). ICG severity explained approximately 1% of total MoCA scores above and beyond demographic measures, diagnosis of depression and time since loss. (Table 4.)

Discussion

Summary of major findings

Complicated Grief was associated with somewhat lower levels of cognitive function compared to control participants after controlling for age, sex, and education. Although differences in global scores were statistically significant they were modest; their clinical significance is not clear. Compared to control participants, those with CG displayed greater decrements in the attention/concentration and visuospatial domains. Age, sex and education accounted for the majority of the variance in cognitive functioning while CG symptoms accounted for a smaller percentage of the variance. Although individuals with CG displayed high rates of major depression, depression accounted for very little of the variance in cognitive functioning.

We would not have been surprised to find clinically significant cognitive deficits in those with CG, given the immense and chronic level of distress these individuals experience. However, in this relatively young sample cognitive decline would not necessarily be expected. Somewhat unexpectedly, the sub-analysis examining participants age ≥ 60 years yielded no group significance. This may reflect differences in our archival control group which may have had participants with caregiver stress and burden.

Study novelty

This study adds to current knowledge by evaluating multiple domains of cognition in the largest clinical sample of help-seeking individuals with CG to date^{25,26, 27}. Moreover, studies that have assessed global cognitive functioning in CG have relied on the MMSE, which does not assess executive function.^{28, 29, 30}.

Comparison to previous literature

Using the MMSE in a community-based sample, Newson et al.³¹ found modest difference in global cognitive functioning between normal griever M=27.43 (2.2) and those with CG M=26.98 (2.4) ($F(1,1086)=5.38, p<0.05$). Also using the MMSE, O'Connor et al.³² showed slightly greater differences in cognitive functioning when comparing both non-bereaved M=28.5 (1.7) and normally bereaved M=27.9 (2) control groups to CG participants M=26.5 (3.5) ($F(2,72) = 4.25, p = 0.02$). Similar to our analysis, both studies showed statistically significant, albeit small, global cognitive deficits among CG participants compared to control participants.

Using the emotional-counting Stroop (ec-stroop) task, O'Connor et al.³³ found that CG participants had longer reaction times across 3 blocks of grief-related words compared to control participants. Maccallum et al.³⁴ found similar results. The ec-stroop task measures attentional bias, a specific function within the domain of attention/ concentration. O'Connor et al. also found no difference among groups in working memory or set-shifting (an aspect of executive functioning). In addition to global cognitive functioning, our results are consistent with O'Connor et al. in the following ways. CG participants showed deficits in the attention/ concentration domain, but did not differ from control participants with regard to executive functioning and memory. Cognitive deficits were independent of MDD. Beyond the domain of attention/ concentration; our findings highlight the possibility that aspects of the visuospatial domain may be impaired in some individuals with CG.

Study limitations

Because a MoCA score of less than 21 was an exclusion criteria in the HEAL study we were unable to capture individuals with CG who were most impaired cognitively. A wider range of MoCA scores may increase the effect sizes of the predictors in the statistical models used. However, this would likely add individuals with dementia to the group. Because CGT has not been developed and tested for use in persons with dementia we needed to exclude all such individuals in the primary study (HEAL). This is why a cutoff score of less than 21 was a criteria for exclusion. Even so, very few persons initially screened had MoCA scores of less than 21.

Although a widely used clinical screening tool for dementia, the MoCA is neither as sensitive nor specific in evaluating neurocognitive impairment or dementia as thoroughly as a comprehensive neuropsychological battery.

We also did not sample a control group recruited to match our CG participants but used an archival control group that differed from our CG group in terms of time of recruitment and possible psychiatric morbidity. Because our control group consisted of friends and spouses of patients with Huntington's disease, Alzheimers disease, MCI and other illnesses, we cannot rule-out the possibility that they may have experienced elevated levels of caregiver stress and burden thus negatively impacting their cognitive performance. Furthermore, it is possible that individuals in the control group were bereaved or suffering from CG. A small percentage of our control participants were relatives of those with Huntington's disease,

Alzheimer's disease, and multiple sclerosis. Therefore, we also cannot be certain of the extent to which genetic factors contributed to cognitive performance in the control group.

Although we did control for education level in our analyses, premorbid IQ was not measured and thus could not be controlled for. Education, like premorbid IQ, has been shown to be an important predictor of performance on cognitive screening tests including the MoCA³⁵.

Implications for future studies

This exploratory and descriptive analysis adds to the growing literature exploring cognitive functioning in CG. These data point to the need for further research in cognitive health as it relates to CG, specifically with regard to the attention/concentration and visuospatial neurocognitive domains.

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Contributions: Dr. Reynolds and Mr. Hall designed the study and prepared the manuscript. Dr. Butters provided expertise in the analysis and interpretation of neuropsychological data. Dr. Corey-Bloom provided control data for comparison purposes with MOCA scores obtained in participants with complicated grief. Amy Begley undertook the statistical analyses. Christine Mauro participated in statistical analyses and data presentation. Drs. Shear, Simon, Lebowitz, and Zisook all had critical input into the development and revision of the manuscript, and all participated in the design of the parent study, HEAL, a multisite clinical trial sponsored by the National Institute of Mental Health. All authors contributed to and have approved the final manuscript.

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Highlights

1. We compare performance on the MoCA in persons with CG and an archival control group.
2. Individuals with CG displayed mild deficits in global cognitive functioning.
3. Deficits were observed in the attention and visuospatial neurocognitive domains.
4. Age, sex and education accounted for much of the variance in MoCA scores.
5. Very little MoCA score variance was due to CG severity, chronicity or current MDD.

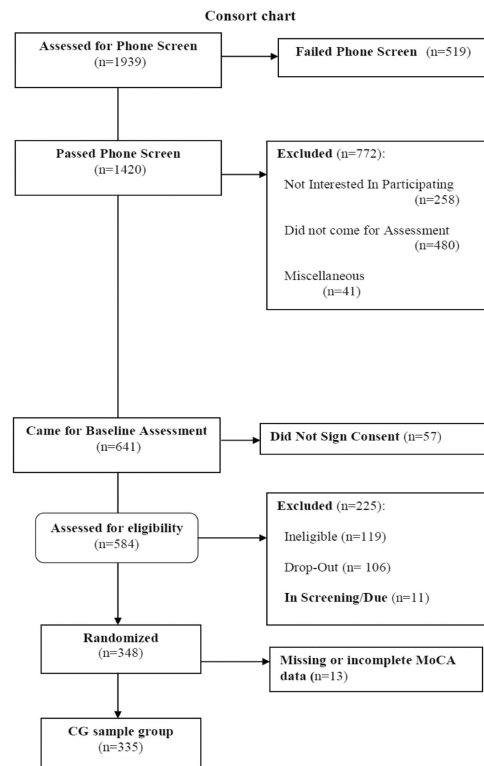


Figure 1.

Table 1

Demographic Measures

	Complicated Grief (CG) [n if reduced sample] N=335	Control [n if reduced sample] N=250	
Age	53.01 (14.57) Median =55 Range =19–89	54.42(19.81) Median=57 Range=20–89	t(583)=−0.99, p=0.32
%Female	79.70 (n=267)	53.60 (n=134)	chisq(1) = 45.24, p<0.0001
Race	[n=326]	[n=185]	Fisher exact p=0.01 (White vs. other: Fisher exact p=0.42)
% American Indian or Alaska Native	1.84 (n=6)	0.54 (n=1)	
%Asian	1.84 (n=6)	5.95 (n=11)	
%Black	10.43 (n=34)	5.41 (n=10)	
%Native Hawaiian or Other Pacific Islander	0.61 (n=2)	0.00 (n=0)	
%White	85.28 (n=278)	88.11 (n=163)	
Education Level			chisq(3) = 2.60, p=0.46
%<= 12 yrs	12.54 (n=42)	14.80 (n=37)	
% 13–15yrs	34.03 (n=114)	33.60 (n=84)	
% 16 yrs	21.79 (n=73)	25.20 (n=63)	
% > 16 yrs	31.64 (n=106)	26.40 (n=66)	
Site			
%San Diego	28.85 (n=100)	--	--
% Boston	27.46 (n=92)		
%New York	11.04 (n=37)		
%Pittsburgh	31.64 (n=106)		

Table 2

Clinical Measures

	Complicated Grief (CG) N=335
Time Since Loss	4.74 (7.19) Median = 2.37 Range=0.50–58.67
Inventory Complicated Grief (ICG score)	43.05 (8.96)
Quick Inventory of depressive symptomatology self-report (QIDS-SR)	13.46 (4.22)
%Current MDD	66.57 (n=223)
Cumulative Illness Rating Scale (CIRS)	
Total	6.27 (4.31)
Number of affected organ systems	4.70 (2.75)
Heart + Vascular	0.93 (1.15)
Neurological	0.44 (0.64)

Table 3**MoCA Scores**

	Complicated Grief (CG) N=335	Controls (CTRL) N=250	Age F,p/χ^2,p	Sex F,P/χ^2,p	Education F,p/χ^2,p	CG F,P/χ^2,P
MoCA Total* (range=0–30)	26.79 (2.20) Median=27 Range=21–30	27.12 (2.24) Median=28 Range=21–30	57.42, p<0.001	5.39, p=0.02	9.78, p<0.0001	9.11, p=0.003
Domains Executive Functioning (range=0–4)	3.46 (0.76) Median=4 Range=1–4	3.53 (0.66) Median=4 Range=1–4	13.21, p=0.0003	2.89, p=0.09	31.51, p<0.0001	2.46, p=0.12
Visuospatial (range=0–4)	3.41 (0.74) Median=4 Range=1–4	3.63 (0.59) Median=4 Range=2–4	20.38, p<0.0001	3.74, p=0.05	7.32, p=0.06	12.52, p=0.0004
Language (range=0–5)	4.65 (0.59) Median=5 Range=2–5	4.55 (0.72) Median=5 Range=2–5	6.01, p=0.01	3.95, p=0.05	9.35, p=0.03	0.62, p=0.43
Short term memory (range=0–5)	3.79 (1.18) Median=4 Range=0–5	3.74 (1.34) Median=4 Range=0–5	47.61, p<0.0001	12.61, p=0.0004	1.79, p=0.62	2.41, p=0.12
Attention/Concentration (range=0–6)	5.56 (0.76) Median=6 Range=2–6	5.72 (0.62) Median=6 Range=2–6	3.80, p=0.05	2.06, p=0.15	13.66, p=0.003	6.39, p=0.01
Orientation (range=0–6)	5.92 (0.31) Median=6 Range=4–6	5.95 (0.24) Median=6.00 Range=4–6	1.23, p=0.27	0.03, p=0.86	3.14, p=0.37	1.99, p=0.16

F statistic reported for ANCOVA (df=1,578) and χ^2 (df=1) reported for the domains scores.

* No point added for participants with $\leq$ High School education

Table 4

Results from linear regression looking at effects of depression and CG severity

Model:F(9,325)=5.57, p<0.0001, R-square = 0.1337						
	Parameter Estimate	Standard Error	t Value	p-value	Standardized Estimate	%Variance Explained
Intercept	29.77	0.77	38.87	<0.001	0	--
Age	-0.03	0.02	-3.61	<0.001	-0.20	3.4
Female	0.28	0.28	0.99	0.32	0.05	0.2
ED: <= 12yrs	-1.54	0.39	-3.92	<0.001	-0.23	4.0
ED:13-15yrs	-0.93	0.28	-3.27	0.001	-0.20	2.8
ED: 16yrs	-0.35	0.32	-1.10	0.27	-0.07	0.3
Site:NY	-1.00	0.39	-2.60	0.01	-0.14	1.8
Current MDD Dx	0.16	0.26	0.61	0.54	0.03	0.0
Time Since Loss	0.01	0.02	0.77	0.44	0.04	0.1
ICG score	-0.03	0.01	-1.93	0.06	-0.11	1.0