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Amygdala but not Hippocampal Damage Associated with Smaller Social Network Size

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Abstract

Social network size has been associated with complex socio-cognitive processes (e.g., memory, perspective taking). Supporting this idea, recent neuroimaging studies in healthy adults have reported a relationship between social network size and brain volumes in regions related to memory and social cognition (e.g., hippocampus, amygdala). Lesion-deficit studies in neurological patients are rare and have been inconclusive due to differences in participant sampling and measurement. The present study uses a multiple case study approach. We investigated patients with focal damage to the hippocampus and/or amygdala (two neural structures thought to be critical for social networks), and examined the patients' social network size, loneliness, and life satisfaction relative to a non-injured comparison group. Patients with amygdalar damage had smaller social networks and reported higher levels of loneliness and

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Declaration of Interest Statement

The authors report no conflicts of interest.

Credit Author Statement

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lower life satisfaction, on average, than comparison participants. Patients with damage to the hippocampus reported more friends than the comparison participants, but did not differ in their ratings of loneliness or life satisfaction. This lesion study offers new evidence that the amygdala is critical for social networks, life satisfaction, and reduced loneliness.

Keywords

social networks; lesion studies; loneliness; amygdala; hippocampus

Understanding the neural and psychological mechanisms of social relationships is vital because of the association with greater health and well-being (Cacioppo et al., 2002; Rafnsson et al., 2015). For example, individuals with high quality, large social networks are at a lower risk for health-related issues, such as heart disease, and have lower levels of stress (Ellwardt et al., 2020; Valtorta et al., 2016). Furthermore, larger social network size and increased contact with one's social network are positively associated with greater future life satisfaction and quality of life in adults, even when controlling for factors such as long-term illness and socioeconomic factors (Rafnsson et al., 2015). One of the proposed mechanisms for individual differences in social network size, or the number of individuals in one's network, is variability in cognitive and social capacities (Stiller & Dunbar, 2007). These differences in socio-cognitive abilities are thought to be reflected in brain structure, as larger regional brain volumes in specific areas are associated with larger social network sizes (Bickart et al., 2011; Hampton et al., 2016; Heide et al., 2014; Kanai et al., 2012; Kwak et al., 2018; Lewis et al., 2011; Noonan et al., 2018; Sato et al., 2016; Spagna et al., 2018; Taebi et al., 2020; but see Lin et al., 2020).

Brain regions important for emotion, social behavior, and memory have been associated with individual differences in social network size. Neuroimaging studies in healthy adults have demonstrated that social network size is positively associated with brain volumes in regions related to mentalizing and social processing (Bickart et al., 2011; Blumen & Verghese, 2019; Kanai et al., 2012; Lewis et al., 2011; Peer et al., 2021). Researchers have also found a positive association between social network size and memory-related brain regions (Bickart et al., 2011; Heide et al., 2014; Kanai et al., 2012). For instance, the entorhinal cortex, which plays an important role in associative memory, was found to be correlated with real-world (Heide et al., 2014) and online social network size (Kanai et al., 2012). There is also growing evidence that the hippocampus may play an important role in helping individuals map social space (Montagrin et al., 2018). Furthermore, Bickart and colleagues (2011) found that in older adults, the volume of the left hippocampus was associated with social network complexity (i.e., the number of different social groups to which each individual belongs). Although there is growing evidence for the involvement of the hippocampus in social network size, it may be that the amygdala plays a more central role, due to its involvement in critical aspects of emotion and social processing.

One of the most robust findings to date is that amygdala volume is positively associated with social network size in healthy adults (Bickart et al., 2011; Heide et al., 2014; Kanai et al., 2012) and extends to both real world and online social networks (Kanai et al., 2012).

There is also evidence that in healthy adults the amygdala may serve as a hub for the social brain (Li et al., 2018). Taken together, these neuroimaging studies suggest that several core regions important for socioemotional and memory processing (amygdala and hippocampal/entorhinal cortex) are positively associated with social network size.

While neuroimaging studies of healthy adults provide insight into brain regions that are involved in a specific process, studies of patients with focal brain damage can help uncover which brain regions are critical for a particular function. Case studies of patients with hippocampal damage and severe, anterograde amnesia provide a window into how impaired memory may manifest itself in patients' social lives (Rosenbaum et al., 2014). In her discussion of previous case studies of patients with hippocampal amnesia, such as the famous cases of HM and SS, Tate highlights the degree to which their social relationships are greatly reduced (Tate, 2002). These individuals often remain isolated due to their memory impairment, have small social networks, and have difficulty making new friends (Corkin, 2013; Tate, 2002; Wearing, 2006). In a multiple case study of two patients with temporal lobe epilepsy who had severe autobiographical memory deficits, the patients reported how the lack of rich personal memories negatively impacted their relationships with others, as they lacked memory for shared experiences, which caused them to feel disconnected and socially isolated from others (Zeman, et al., 2018). On the other hand, two other case studies of women with hippocampal damage demonstrated some success in maintaining and cultivating interpersonal relationships (Duff et al., 2008; Warren et al., 2012). In the case study by Warren and colleagues (2012), the patient had substantial interaction with friends and family whom she knew prior to the injury, but she had made no new friends since the injury. In contrast, the case reported by Duff and colleagues (2008) found that the patient had made and maintained several new personal and meaningful relationships, including her spouse. These case studies suggest that social outcomes may be partially determined by demographic factors such as sex and may vary across amnesic individuals.

Although case studies of hippocampal damage are informative, patient studies that directly assess social network size can provide quantitative information about how the hippocampus is related to social network size. Only two studies have systematically examined the effects of damage to regions implicated in social network size (Becker et al., 2012; Davidson, et al., 2012). Davidson and colleagues (2012) investigated the association between hippocampal damage and social network size. The three patients in the sample consisted of (1) two males in their 60s with broad damage to the medial temporal lobe (hippocampus, parahippocampal cortex, amygdala, and, in one, orbitofrontal cortex) due to traumatic brain injury or herpes simplex encephalitis (HSE) and (2) one female in her 20's with abnormal development of the hippocampus and major output (i.e., fornix, mammillary bodies), likely of congenital origin (Rosenbaum et al., 2014). One of the male patients had made no new friends since the injury, and the other male had only made one friend. The female patient had fared better than the males, having made two new relationships outside of her family (which is within the lower end of the normal range for that sample). As a whole, all three patients were less involved in social activities, such as volunteering or visiting with neighbors than normal. This finding was interpreted to be a consequence of their reduced episodic memory which may be necessary to interact socially and develop friendships.

Case studies of patients with focal amygdalar damage suggest that these patients have substantial interpersonal difficulties in their daily lives (Feinstein et al., 2016). For instance, SM has experienced many difficulties maintaining relationships with friends and significant others (Feinstein et al., 2016; Tranel & Hyman, 1990). In terms of romantic relationships, she is a single mother to three children, and no longer speaks to either her children or partners. She is also very trusting of others, and this could lead her to develop relationships with others who don't have her best interests at heart.

Lab-based studies of patients with amygdalar damage have systematically characterized some of their social difficulties (Adolphs et al., 1998; Adolphs et al., 2005; Becker et al., 2012). For instance, they have confirmed that the amygdala is important for judging trustworthiness (Adolphs et al., 1998) and for the experience of fear (Adolphs et al., 2005). A study by Becker and colleagues (2012) investigated the effects of amygdala damage on social network size. The study examined two female, monozygotic twins with bilateral amygdala degeneration due to Urbach Wiethe disease which results in slowly progressing amygdala damage over time (often beginning in youth) due to lipoid proteinosis. This study produced mixed results: Patient 1 reported a social network similar to that typically found in healthy comparison participants, whereas Patient 2 reported a social network that was on the low end of the normal spectrum (Becker et al., 2012). Furthermore, when using a composite score of the Social Network Index, Patient 2 had the lowest score out of all participants. The two patients differed in their social processing in several ways which may help to explain the differences in social network size. For instance, Patient 1, who had a relatively normal social network, also had intact fearful face recognition and modulation of the acoustic startle response to scenes designed to evoke fear. Patient 1 also demonstrated potentiated responses to fearful faces in the left premotor cortex and bilateral inferior parietal lobule, regions thought to be involved in the mirror neuron system which may play a role in social capacities such as empathy. This finding was interpreted as evidence for compensation of other social processing areas in response to the damaged amygdala and points to the amygdala as a critical neural structure in social network size, when there is little compensatory functioning.

The two lesion studies focused on social network size provide a foundation for understanding the brain regions that are necessary to support social networks. However, these studies are not without limitations. For instance, these studies had small patient sample sizes (Davidson et al.: N=3; Becker et al.: N=2), with variability in patient age, sex, and lesion etiology. In addition, in the study by Davidson and colleagues, two of the patients had broader damage to other regions in the socioemotional circuit (e.g., amygdala and orbitofrontal cortex), making it difficult to draw conclusions about the specific role of the hippocampus in social network size. Furthermore, these studies used different measurement tools to assess social network size, making comparisons among patient types and to other studies in the literature challenging.

While social network size has been an expedient way to measure social functioning, it is not the only variable important for social health and well-being. For example, in addition to the number of an individual's social relationships, their perceptions about the quality of these relationships can influence their life satisfaction and health (Cacioppo et al., 2002; Rafnsson

et al., 2015). One way in which perceptions about relationships can be assessed is through measuring the degree to which an individual feels lonely. Several studies have pointed to an important role for loneliness in determining health outcomes (Cacioppo et al., 2002; Hawkley et al., 2006; Paul et al., 2006). For example, individuals with high loneliness tend to have poorer health and are at higher risk for developing diseases, such as Alzheimer's disease (Hawkley et al., 2006). Because social network size and loneliness are not always correlated (e.g., you can have a large social network size but still feel lonely) it is important to consider both to get a more nuanced picture of an individual's relationships and how they feel about them. Of note, neither Davidson et al. (2012) nor Becker et al. (2012) investigated these factors.

The present study builds upon the previous literature by comparing the relationship between damage to the amygdala and hippocampus and social network size and composition. Another departure from previous studies is the inclusion of patients with focal damage to these regions; previous studies have included patients with more diffuse damage extending into other regions associated with memory and social cognition, such as the ventromedial prefrontal cortex. Due to evidence from previous case studies that there may be differences in social network size as a function of sex and marital status, we examine differences in these categories in each patient group (Duff et al., 2008; Rosenbaum et al., 2014; Warren et al., 2012). Finally, we extend previous studies by including measures of well-being, specifically patients' loneliness and life satisfaction. We compare the size versus the interconnectedness of a patient's network to obtain a more complete picture of the patient's social interactions.

It was hypothesized that patients with damage to the amygdala would have a smaller social network size than patients with damage to the hippocampus and non-injured comparison participants (based on Bickart et al., 2011; Feinstein et al., 2016; Heide et al., 2014; Kanai et al., 2012). Secondly, it was hypothesized that patients with damage to the hippocampus would have a smaller social network size than comparison participants (based on Corkin, 2013; Tate, 2002; Wearing, 2006). We predicted that the patients with damage to the amygdala would have the highest ratings of loneliness because they were expected to have the smallest social networks, followed by slightly lower ratings in the hippocampus group, with the comparison group predicted to have the lowest ratings. Similarly, we hypothesized that the amygdala group would have the lowest levels of life satisfaction, followed by slightly higher ratings in the hippocampus group, and with the comparison group having the highest ratings.

Materials and Methods

Participants

This study was approved by the University of Iowa Institutional Review Board, and informed consent was obtained from all participants. We employed a multiple case study approach to examine the role of the amygdala and hippocampus for social network size and density, loneliness, and life satisfaction. There were 7 patients with focal damage to the hippocampus, 2 patients with focal damage to the amygdala, and 2 patients with damage including both the hippocampus and amygdala. Next, we will describe the patients in detail.

Given previous work suggesting that demographic factors such as sex and marital status may influence our variables of interest, we report these factors here and in the results.

Patients with focal amygdala damage.

Two patients had focal, bilateral damage to the amygdala due to Urbach Wiethe disease, a progressive degenerative disease that is associated with onset of amygdala damage at approximately 10 years of age. These two female patients were patient 2405 and 46 (Adolphs, et al., 1998; Feinstein et al., 2016; Feinstein et al., 2011; Tranel & Hyman, 1990). At the time of testing, 2405 was a young adult (30 years of age), and patient 46 was middle-aged (49 years). 2405 was college educated, whereas 46 had completed high school. Both patients were not married at the time of testing. For additional demographic details see Table 1.

Patients with focal hippocampal damage.

There was a total of 7 patients with focal hippocampal damage (see Table 1 for group level demographic information). This damage was primarily due to an anoxic/hypoxic event or status epilepticus. One patient had unilateral right hippocampal damage from HSE. The extent and location of the brain damage in these patients, as well as their neuropsychological performance has previously been characterized (e.g., Allen et al., 2006, see below). On average, the lesion onset occurred in late middle-age. There were two females in this group (1846 and 2571), and both were 51 years of age (Warren et al., 2012). Patient 1846 had some college, whereas patient 2571 had obtained a college degree. The rest of the group consisted of five males (2563, 2363, 3139, 1465, 2997) who were older adults ranging in age from 58–84 years (M=65.8, SD=10.6). Their education levels ranged from some college to post graduate degrees. Three of the males were married (3139, 1465, 2997), one of the males was widowed (2363), and one male was never married (2563). The two females (1846 and 2571) were both married. All participants who were married or widowed had married prior to the onset of their hippocampal damage.

Patients with damage to the amygdala and hippocampus.

The study included two patients with bilateral damage to the amygdala, hippocampus, and other regions of the medial temporal lobe (2308 and 1951) due to HSE (for additional case details, see Feinstein et al., 2010). On average, the lesion onset occurred around 36 years of age. At the time of testing, both patients were older adults (2308: 58 years; 1951: 62 years). Both patients had at least a college degree, with 2308 holding a graduate degree. Neither patient had married.

Non-injured Comparison Participants.

We compared data from the patients to a group of 102 non-injured comparison participants (NC group) who had similar demographics to the patients (i.e., age, sex, and education), and did not have a history of neurological or psychiatric disease. Each patient was matched to at least one comparison participant on sex (male or female), age (+/− 5 year range), and education (+/− 2 year range).

Neuropsychological Assessment.

The patient groups were compared on several neuropsychological measures assessing intelligence, memory, and language (please see Table 2.) Neuropsychological testing included measures of intelligence (Wechsler Adult Intelligence Scale-III), memory (Wechsler Memory Scale-III-General Memory Index), language (Boston Naming Test, Token Test), and depression (Beck Depression Inventory) (Beck et al., 1961; Benton et al., 1994; Kaplan et al., 1983; Wechsler, 1997a; Wechsler, 1997b). Patients performed within normal limits on measures of intelligence and language. Patients who had either focal hippocampal damage or damage to the hippocampus and amygdala demonstrated severe declarative memory impairments with variability across the group in memory severity, as measured by the Wechsler Memory Scale-III, General Memory Index. One of the patients with focal amygdala damage had normal declarative memory performance. (The other patient with amygdala damage was not available to complete all of the neuropsychological measures). The majority of these patients are well known to our group and have been studied extensively as part of their participation in Patient Registry of the Division of Behavioral Neurology and Cognitive Neuroscience at the University of Iowa. (For additional neuropsychological and neuroanatomical characterization please see: Adolphs & Tranel, 2000; Allen et al., 2006; Feinstein et al., 2016; Tranel & Hyman, 1990; Warren et al., 2012).

Lesion Location Characterization.

Lesion location was confirmed by structural magnetic resonance imaging (MRI) when possible. For patients with hippocampal lesions, high-resolution volumetric MRI analyses showed reduced hippocampal volumes compared to aged-matched comparison subjects. For patients with hippocampal damage due to anoxia or status epilepticus (1846, 2363, 2571, 2997) hippocampal volumes, reported as studentized residuals relative to the comparison sample, were −4.23, −2.64, −1.01, and 0.57, respectively (Allen et al., 2006; Warren & Duff, 2012). For anoxic patients 2563 and 3139, high-resolution volumetric MRI measurements are unavailable due to contraindications for MRI (e.g., pacemakers); lesion localization was based on computerized tomography. Patient 1465 has focal hippocampal damage due to HSE with near-complete right hippocampal damage, but a largely intact left hippocampus and a hippocampal volume of −2.95 (Warren & Duff, 2012). There is no evidence of amygdala damage in any of these patients. Available MRI images for patients 1846, 2363, and 2571 are shown in Figure 1.

Detailed neuroanatomical descriptions of patient 46 from previous studies reveal extensive bilateral damage to the amygdala, while the hippocampus proper appears entirely intact (e.g., Adolphs et al., 1998; Feinstein et al., 2016). More recent imaging, closer in time to the current study, also revealed additional lesions located in the putamen (Feinstein et al., Tranel, 2011). Like patient 46, patient 2405 has bilateral damage to the amygdala, secondary to Urbach Wiethe disease. Available MRI images for patients 46 and 2405 are shown in Figures 2A and 2B, *respectively*.

For patients with damage to the hippocampus and amygdala (1951, 2308), MRI images are shown in Figure 1. High-resolution volumetric MRI analyses were performed on patient 1951 and showed hippocampal volumes decreased by −8.10 compared to aged-matched

comparison subjects (Buchannan et al., 2005). Both patients have extensive damage to the hippocampus, amygdala and other medial temporal lobe cortices bilaterally (see Cavaco et al., 2012; Feinstein et al., 2010). Patient 1951's lesion extends into the right temporal lobe including the right temporal pole. Patient 2308's lesion extends into the left temporal lobe including the left temporal pole.

Measures

Social Network—Social network size and relationship closeness was measured by the National Social Life, Health, and Aging Project Social Network Module (Cornwell et al., 2009). First, participants were asked to generate the names of the people in their life that they consider to be important to them. Specifically, the prompt was, "Looking back over the last 12 months, who are the people with whom you most often discussed things that were important to you?" Following this, the participants rated each person in the network based on closeness (1=not very close, 4=extremely close), and frequency of talking with this person (1=daily, 8=less than once a year). Participants also completed four questions based upon the degree to which they engaged in social participation in their communities on a scale from 1=several times a week, to 7=never.

We also calculated the density of the participants' social networks. Participants were asked to indicate how frequently they were in contact with each person in their social network and how frequently each person in their network was in contact with each other. The highest possible frequency of contact was daily, and the lowest possible frequency of contact was never. The maximum score on the density measure=.5 which was indicative of a highly connected social network. These data were then entered into a social network plotting program called, "Social Networks Visualizer," (http://socnetv.sourceforge.net) allowing us to create network maps for each participant.

Loneliness—To measure perceived loneliness, participants completed the UCLA Loneliness Scale–Version 3 (Russell, 1996) which measures one's subjective perception of the degree of loneliness one experiences, on average, on a daily basis. This scale contains 20 items in which individuals respond to the statements by indicating on a 4-point scale the following responses: 1=Never, 2=Rarely, 3=Sometimes, or 4=Always feel, in the manner listed in the statement. A few example items are: "How often do you feel alone?"; "How often do you feel close to people?" There is a mix of positively and negatively worded items, with the negatively worded items reverse scored. Total scores are calculating by summing all of the item responses. Scores can range from 20–80, with higher scores indicative of greater loneliness. This scale has high test-retest reliability (over 1 yr., r = .73; Russell, 1996). Additionally, it demonstrates high internal consistency (α = .89 - .94). Undergraduate students typically report scores ranging from 20–74 (N = 487, M = 40.08, SD = 9.50; Russell, 1996).

Life Satisfaction—The Life Satisfaction Index A is a short, self-report measure of an individual's satisfaction with their own life (Neugarten et al., 1961). This scale includes a series of statements related to an individual's level of happiness and satisfaction. Our scale included 7 items from the original Life Satisfaction Index A scale. To each item, the

participant responds with one of the following: “disagree, uncertain, or agree.” Participants receive 1 point if their response matches the scoring guide for that item; they receive 0 points if their answer does not match the scoring guide. Responses to all items are then summed to create a total score, with a maximum score of 7 points. Higher scores indicate greater happiness or satisfaction with one’s present life. A few examples from this scale include: “These are the best years of my life”; “I am just as happy as when I was younger.”

Informant: Close Other & Family Member Responses—It is well-established that patients with damage to the hippocampus suffer from severe, declarative memory impairments (Scoville & Milner, 1957), and this could potentially interfere with their ability to complete the questionnaires with accuracy, particularly those that require reviewing the recent past to assess life satisfaction or with whom they have been in contact. In addition, patients with amygdala damage may experience changes in social cognition and self-awareness that could also impact their accurate reporting on the questionnaires. Thus, when possible, family members or close others of these patients completed the questionnaires about the patients to serve as a point of comparison. The family members and close friends’ ratings about the patients are designated as the informant reports. This approach of comparing patient and close others’ scores has been frequently utilized in research on neurological patients as a means of assessing the veracity of patient responses (Beadle et al., 2013; Gilboa et al., 2006; Hornberger et al., 2014; Ruby et al., 2007; Sollberger et al., 2014; Zamboni et al., 2010). In terms of selecting a close other/family member, the person rating the patient was required to be a family member (e.g., spouse, parent, child, sibling, grandparent, aunt or uncle) or close friend who had known the patient for more than 10 years and also knew them before and after the brain injury. The patient was asked to identify a close other/family member who might be willing to participate in the study. Following this, the research assistant in the lab called this person, told them about the study, and asked whether they would be willing to participate. If they were willing to participate, the close other/family member completed a consent form and then filled out the questionnaires on loneliness and life satisfaction based on the way the patient behaved in their daily life. For the NSHAP interview, the close other/family member completed a phone interview with the research assistant in which they responded based upon what they knew about the patient’s current social network.

Results

Social Network Size, Loneliness, and Life Satisfaction.

Non-injured Comparison Participants.—The non-injured comparison participants (NC) had, on average, 6 friends in their network (M=5.62, SD=3.30, median=5, range: 1–19). On average, healthy women (N= 59) had more friends (M=6.17, SD = 3.66) than healthy men (N = 43; M = 4.86, SD = 2.60). There was no significant relationship between age and social network size in the healthy comparison participant sample [$t(101)= -.04$, p=.70]. Half of the people that NC participants consider to be important to them were from their nuclear family (56.32%). The average density of their network was .42 (SD=.08). They reported an average level of closeness with others of 3. The frequency with which they talk to others they consider to be important to them was approximately 3, reflecting interactions

with close others every week. Their average social participation was 3.9, which reflects participation several times a year. Their loneliness scores, on average, were not in the highly lonely range, which is 45 points or greater on the scale (*M*=37.3). However, 22% of the healthy comparison participants did have scores in the highly lonely range. The NC group had average life satisfaction levels of 3.2 out of a maximum score of 7, reflecting moderate levels of life satisfaction. For additional information comparing men and women on these measures, see Table 3.

Patients with damage to the hippocampus

Females with damage to the hippocampus: There were two females with damage to the hippocampus in our sample. Patient 1846 reported having 5 friends in her social network, which was consistent with the informant's report of 6 friends. Patient 2571 reported having 14 friends in her social network (no informant was available to report about 2571). The number of friends in 1846's network is similar to the average of women in the comparison sample (M=6.17), whereas the number of friends reported by 2571 is greater than the comparison sample. See Figure 3 for mean level comparisons to the non-injured comparison participants. For 1846, 66.67% of her social network was made up of nuclear family members, and the informant also corroborated the veracity of this report. In comparison, for 2571, 100% of their social network was made up of family. In terms of the density of their networks, both 1846 and 2571 reported high network density of 0.5 (which was corroborated by 1846's informant); see Figure 4 for density maps.

Both 1846 and 2571 reported that they felt, "very close," to their social network which was corroborated by 1846's informant who reported the same score. Results were less consistent in terms of the frequency with which they spoke to their social network members. Patient 1846 reported a frequency of contact of approximately, "several times a week," whereas the informant reported, "approximately once a week." In contrast, patient 2571 spoke to their network, "approximately once or twice a year." In terms of social participation in the community, 1846 reported engaging with the community, "approximately about once or twice a year," (which was the same as their informant). 2571 reported about once a month.

In terms of loneliness, both patients reported moderate levels of loneliness. Note that scores of 45 or higher are considered highly lonely. 1846 reported a loneliness score of 43, whereas their informant rated them as lonelier with a score of 47. 2571 reported a score of 29. Women from the comparison sample reported, on average, a loneliness score of 36.33 which is in between the loneliness scores of these two patients. In terms of life satisfaction, both patients reported moderate levels of life satisfaction. However, the informant's rating was not consistent with patient 1846, as they perceived patient 1846 to have little to no life satisfaction.

Males with damage to the hippocampus: The size of the social network for the five males with damage to the hippocampus ranged from 5–11 individuals in their network (see Table 3 and Figure 3). In comparison, men from the healthy adult group reported on average approximately 5 friends (SD= 2.60, range: 1–13) which is consistent with the low end of the range for the patients.

Males with hippocampal damage who were married

Patient 3139 reported having 7 individuals in his social network (informant reported 9). Patient 2997 reported having 11 friends total (informant reported 9). Whereas 3139 and 2997 were in their 60's, 1465 was the oldest patient in this group at 84 years of age which could have influenced their social network size. Patient 1465, the oldest participant, reported having 5 people in his social network (informant reported 3). These three male participants reported that 28.6% - 66.7% of their social networks were made up of nuclear family members. Patient 3139 reported that 28.6% of their network was made up of nuclear family (informant reported 33.3%), patient 2997 reported 63.6% (informant reported 66.7%), and patient 1465 reported 66.7 % (informant reported 75%).

All three male patients with hippocampal damage reported that their social networks had a high level of density, meaning that the individuals in the network interacted with each other with some frequency. Their scores ranged from 0.4–0.5 density, with 0.5 being the highest density level possible (see Figure 4). For patient 3139, both the patient and informant rated the density of the network as 0.5. Similarly, patient 1465 reported a density of 0.4 (informant reported 0.5) and patient 2997 and their informant reported a density of 0.4.

In terms of their perceptions of closeness to individuals in their network, the patients reported that they felt either, "extremely close" or "very close." The informants of these patients rated the patients as slightly less close than the patient's themselves reported. For instance, 3139 reported a closeness of, "extremely close," whereas the informant reported a closeness of, "very close." Similarly, patient 1465 reported a closeness level of, "very close" (informant reported a closeness level of, "somewhat close.") Patient 2997 rated their level of closeness as, "extremely close," whereas the informant rated it as "very close."

The patients differed in their frequency of contact with their social networks, ranging from, "several times a week" to "once every two weeks." Patient 3139 reported a frequency of contact of, "several times a week," versus, "every two weeks," by the informant. Patient 2997 interacted with their network with less frequency, "once every two weeks" (informant, "once a week"). For 1465, frequency of contact was reported as, "once a week," for the patient and, "once every two weeks," for the informant.

Social participation in community activities was also assessed. The patients differed in how frequently they participated in community activities, ranging from, "every week," to, "about once or twice a year." In each case, the informant reported that the patient participated slightly less than the patient reported. Patient 3139 reported that they participated in community activities, "every week," (informant reported, "several times a year"). For 1465, social participation was reported as, "about once a month," by the patient (informant reported, "about once or twice a year.") Patient 2997 reported that they participated, "about once or twice a year," (informant: reported, "less than once a year.")

Loneliness and life satisfaction were also examined in the patients. The informants for 2997 and 1465 were not available to complete these two measures. In terms of loneliness, the patients reported moderate levels ranging from 28–40 on the loneliness scale. Specifically, patient 3139 reported a score of 28 (informant reported 44). Both 2297 and 1465 reported

a loneliness score of 40. Patients 3139 and 1465 reported high levels of life satisfaction, whereas 2997 reported a low level of life satisfaction. Patient 3139 reported high life satisfaction with a score of 5. However, the informant rated them as having little to no life satisfaction. Patient 1465 reported the highest possible score on the life satisfaction scale (7). In contrast, patient 2997, reported a low level of life satisfaction (1).

Unmarried men with hippocampal damage

Patient 2563 is the only male participant in the group who never married. He reported having 10 friends in his social network (informant reported 4). Patient 2563 perceives themselves to be very close to the people in their network (informant reported people to be, “not very close”). Patient 2563 reported that he speaks to people in the network, “several times a week,” (informant reported “daily contact”). The patient reported, “several times a year,” on social participation (informant reported participation, “about once or twice a year”). Patient 2563 reported that 40% of his social network was made up of nuclear family members (informant reported 33.3%). The patient reported that the density of their network was moderate (0.3) (informant reported 0.5); see Figure 4.

The patient reported a score of 39 on loneliness, which is indicative of moderate levels of loneliness (informant reported a score of 48, indicative of high loneliness). The patient reported a satisfaction score of 5, while the informant reported a satisfaction score of 0. The patient reported feeling highly satisfied with life, whereas the informant report suggests that they perceived the patient as having little to no satisfaction with life.

Patient 2363 was widowed at the time of the study. He reported having 5 friends (informant reported 4). Patient 2363 rated themselves as, “somewhat close,” with their network (informant rated them as, “very close”). The patient contacted the people in their network, “about once or twice a year,” (informant concurred). The social participation with the community occurred, “several times a year,” (informant rated it as, “never”). Patient 2363 reported that 60% of his network was made up of family members (informant rated it to be 100%). Both the patient and informant reported that the patient’s social network had a high density (.5). 2363 reported that loneliness was at the top of the moderately high level (44) (informant reported 41). The patient reported moderately high levels of life satisfaction, whereas the informant reported that the patient had little to no satisfaction.

Summary of Results for Patients with Damage to the Hippocampus.—Overall, the social network size of patients with damage to the hippocampus is similar to that of healthy comparison participants. Patients with damage to the HC reported social network sizes that fell within the reported range of the healthy comparison group, although, on average, they reported slightly larger social network sizes (HC M=8.14). However, the patients’ reports may be slightly inflated, as the informants rated the HC patients as having an average social network size of 5.83, which is very similar to the average of the healthy comparison group (M=5.62). The patients with hippocampal damage had loneliness scores indicative of moderate-to-high levels of loneliness. Informants for some patients with hippocampal damage reported they perceived higher levels of loneliness than the patients reported. Patients with hippocampal damage largely reported moderate to high levels of life

satisfaction. Of note, however, is that the informants of most patients with hippocampal damage rated them as having little to no satisfaction with life.

Patients with focal damage to the amygdala

Patient 46.: Patient 46 reported having 3 friends (and this same number was confirmed by their informant's rating). In contrast, women in the comparison group reported having 6 friends – double the number of this patient. The patient considers themselves to be very close to the people in their social network (rating on closeness item: 3); see Table 3 and Figure 3. The family member rated them even higher, with a rating of, "extremely close" with the people in their network. In terms of how much the patient interacts with the people in their network, they reported talking to the people in their network once a week which was also confirmed by the family member with a median rating of 3 on this item. For the items assessing social participation in the community, the patient reported being engaged in community activities approximately once a month. In contrast, the family member reported the patient only engaged in this activity approximately once or twice a year.

In the patient's social network, 0% were from the patient's nuclear family (and this same percentage was confirmed by the informant rating). A density analysis was also calculated to examine whether the people in the patient's network interact with each other, and if so, the frequency of their interaction. The density of the patient's social network was .3, but was reported to be slightly higher in density by their informant (.4); see Figure 4. Since the highest possible value of density is .5, this suggests the patient's social network density is moderate but not high. Because there are few lines between the people in the network, this indicates that the individuals within the network do not all interact with each other. Of those who do interact with each other, the thicker, bolded lines indicate that those who do interact, interact fairly often.

Patient 46 reported a loneliness score of 67 points which is in the highly lonely range, and is more than 1.5 times higher than the average loneliness rating by women in the comparison group (M=36.33). The family member rating for the patient was a score of 64, which is similar to the score the patient reported. As a point of comparison, healthy comparison participants (20 out of 91 participants who completed the loneliness questionnaire) who rated themselves as having high loneliness (45 or greater on the loneliness scale) had on average 4.10 friends (SD=2.05), which is similar to the number of friends patient 46 reported (3 friends). When comparing the life satisfaction level of the patient to that of their family member rating, it was found that the ratings were consistent and reflected low levels of life satisfaction [family member of patient 46: 0; patient 46: 1]. On the other hand, the NC group had higher levels of life satisfaction (NC group: M=3.21, SD=1.95).

Patient 2405.: Patient 2405 reported having 3 friends which is fewer than reported by the women in the comparison group (M=6.17). The informant rated them as having more friends (5 friends). The patient perceives themselves to be, "very close," with the people in their network (which is corroborated with the same rating by the informant). In addition, the patient reported speaking with the people in their network, "daily," with the informant reporting a similar response, but with slightly less frequency (i.e., "several times a week").

In terms of social participation more generally, the patient reported social participation rates of, “about once or twice a year,” with the informant reporting social participation rates of, “less than once a year.” Within patient 2405’s network, 40% of the network was composed of nuclear family members. The patient rated the density of their network as high, with a density value of .5, whereas the informant rated it as slightly less dense (.4). In general, the members in patient 2405’s network interacted with each other, with some having frequent interaction. Patient 2405 was not available to complete the questionnaires measuring loneliness and life satisfaction.

Summary of Results for Patients with Damage to the Amygdala.—Both female patients with damage to the amygdala reported a social network size of 3 friends, which was at the lower end of the distribution for healthy comparison participants and smaller than the comparison group average [range: 1–19 (*M*=5.62)]. In particular, women in the healthy comparison group reported having 6 friends, on average, which is double the social network size of the patients with damage to the amygdala. The informant ratings were relatively consistent with the patients’ ratings. Patient 46 reported high levels of loneliness and low levels of life satisfaction relative to women in the healthy comparison group, and these ratings were corroborated by their informant.

Patients with damage to the hippocampus and amygdala: The patients with damage to the hippocampus and amygdala in our sample had the densest amnesia of all of the patients who had hippocampal damage in our sample, with a severe memory deficit similar to other cases of dense amnesia in the literature, such as HM and SS.

Patient 1951: 1951 reported having two friends in their social network (see Table 3 and Figure 3). The family member of patient 1951 reported that the patient had 0 friends or family members that met the criteria in the questionnaire, which suggests their social network may be even smaller than what the patient themselves reported. In contrast, men from the comparison group reported having an average of approximately 5 friends in their social network. Patient 1951 reported that they were, “very close,” to the people in their network, whereas the informant reported that they were, “not very close.” In terms of frequency of contact, the patient reported speaking, “several times a week,” whereas the informant reported that they spoke less than once a year. The patient reported that they were engaged in social participation in the community about once or twice a year, whereas the informant reported that they participated, “several times a year.” The patient reported that their social network was made up 100% of nuclear family, while the informant reported instead that the percentage was 0%. The patient reported that the density of their social network was .5, whereas the density reported by the informant was 0; see Figure 4.

1951 reported a high loneliness score of 56. This loneliness score is higher than the average score reported by men from the comparison group (*M*=38.58). The family member rating for patient 1951, was 38, suggesting that the family member perceived the patient to have lower loneliness than the patient reported. The overall comparison group reported average loneliness levels of 37.32, which is similar to the family member report for 1951, but differed from the patient’s rating. The family member of patient 1951 reported that the patient experienced less life satisfaction than the patient themself reported [family member

AMY+HC: 0; patient AMY+HC: 2]. The comparison group reported a level of satisfaction of 3.21 which is more similar to patient 1951's report.

Patient 2308: The patient reported having 2 friends in their social network (versus *M*=4.86 for men in the healthy comparison group). The patient 2308 passed away during the course of the study and thus data were not available to be collected from their family member. Patient 2308 reported that they were, "very close," to people in their network. They reported that they spoke with people in their network approximately once a week. In terms of social participation, they engaged with community groups approximately once a month. In terms of the makeup of their social network the patient reported that 100% of their network was made up of nuclear family members. The density reported by 2308 was 0.5, reflecting high levels of density in the network. All members of the network interacted with each other and spoke frequently. Patient 2308 reported a loneliness score of 27, which is not in the highly lonely range, and was lower than the average score of the men in the comparison group. In terms of life satisfaction, patient 2308's score was 7 points, which is the highest score on the scale, indicating high levels of happiness or satisfaction with one's current life.

Summary of Results for Patients with Damage to the Hippocampus and Amygdala.—Both male patients with damage to the hippocampus and amygdala reported having a social network size of 2, versus approximately triple that number in the non-injured comparison participant group (M=5.62; range: 1–19). In terms of loneliness and life satisfaction, results were mixed: 1951 reported high levels of loneliness and relatively low life satisfaction, which was confirmed by their informant, while 2308 reported lower levels of loneliness and very high levels of life satisfaction.

Discussion

The goals of the study were to compare whether patients with damage to the amygdala and/or hippocampus (regions of the brain implicated in emotion, social cognition, and memory) had smaller social network sizes, greater loneliness, and poorer life satisfaction relative to a demographically matched, non-injured comparison group. Furthermore, we examined how damage to the amygdala and/or the hippocampus was associated with perceived loneliness and life satisfaction. Understanding how brain damage is related to social relationships is important because it can affect the well-being of the individual and their family (Cacioppo et al., 2002; Courtin & Knapp, 2015; Rafnsson et al., 2015). By determining how brain damage to particular regions may differentially be associated with social relationships, preventative steps (e.g., education and counseling) can be set up for those patients at risk of developing poor social relationships.

Individuals with focal damage to the hippocampus and associated episodic memory impairment were found to have similar social network sizes to those of non-injured comparison participants. This is a somewhat surprising finding given that memory intuitively would seem to help support social interactions in relationships. Importantly, there are discrepancies in the literature on the role of memory in social relationships. The findings here suggest that differences in neuroanatomy may, in part, explain some differences. Previous case studies of patients with larger lesions that include both the

amygdala and hippocampus have suggested that there are reductions in the ability to make and maintain relationships. For instance, the extensively studied patient HM, had a large lesion that included the hippocampus (anterior portion) and most of the amygdala (but not portions of the centromedial nucleus), among other regions in the medial temporal lobe (Annese et al., 2014; Augustinack et al., 2014). HM reportedly had difficulty making and retaining friends (Tate, 2002), although he was capable of developing preferences for some new acquaintances over others (Corkin, 2013). Another study with three patients with hippocampal (but in some cases also amygdalar and frontal) damage also found that one of these patients had a smaller social network (Davidson et al., 2012; Kaushall et al., 1981). In contrast, case studies that have included patients with damage largely restricted to the hippocampus (and no presence of amygdalar damage) report relatively normal social networks (Duff et al., 2008; Warren et al., 2012). However, it is interesting to note that both patients in these two case studies were female, and there is some evidence that biological sex can confer advantages in social cognition, with females having fewer deficits than males after brain injury (Duff et al., 2008; Rigon et al., 2016; Warren et al., 2012). That said, the specificity of neurological damage may be more predictive of social function, as both of the patients with amygdala damage were female and also showed reduced social functioning.

Our finding that patients with amygdala damage, whether restricted or combined with hippocampal damage, have small social networks is consistent with the role of the amygdala in social processing and interaction (Adolphs et al., 2005) and with prior neuroimaging work documenting a relationship between social network size and amygdala volume in healthy adults (Bickart et al., 2011). The results of the present study extend this finding by confirming the relationship in individuals with amygdala damage. That the amygdala would play a critical role in the development and maintenance of social relationships, in humans and other animals, makes good sense. For instance, the amygdala plays a critical role in detecting others' emotional states which is important for social interactions (Adolphs et al., 2005). The amygdala also plays an important role in social attention, or the ability to direct our attention to socially relevant information (Birmingham et al., 2011), as well as judging the trustworthiness of others (Adolphs et al., 1998). It is involved in the experience of our own emotions such as fear, happiness, and sadness (Adolphs et al., 2005; Feinstein et al., 2011; Tranel et al., 2006).

These findings also fit with previous observations in patients with bilateral amygdala lesions and offer a new lens with which to understand the relation between deficits in basic emotional processes documented in the laboratory and how these impairments are related to the development and maintenance of one's social world. Patient 46 has significant problems with social interaction and relating to others in her daily life (Feinstein et al., 2016; Tranel & Hyman, 1990) and displays disruptions in the development and use of common ground in social interaction (Gupta et al., 2011). Patient 46 also shows impaired ability to recognize fearful facial expressions (Adolphs et al., 2005), which may be relevant to social relationships, as they serve as an environmental signal whether it be danger, stress, or bonding. In the Becker and colleagues (2012) study of two patients with amygdala damage, they found that the patient with a smaller than normal social network size, also had difficulties recognizing fear from facial expressions. Furthermore, the amygdala is implicated in the experience of empathy and compassion for others, which is a critical social

emotion for relating to others' experiences (Marsh et al., 2013; for reviews see: Blair, 2007; Blair, 2008; Marsh, 2016). Thus, the current findings suggest that the amygdala is critical for establishing a social network size that is maintained by the majority of healthy non-brain injured adults and fit well with existing data on the importance of the amygdala in social interaction and social network size from other methods. Indeed, it appears that disruption to the amygdala increases one's risk of having a small social network and, by extension, may place such individuals at greater risk for the range of health consequences associated with small social network sizes and loneliness (Cacioppo et al., 2002; Cacioppo & Cacioppo, 2014; Hawkley et al., 2006; Wilson et al., 2007).

We also speculate that the nature of the family relationships in our sample may play a significant role in our findings. Our sample of patients with hippocampal damage have remarkably supportive and involved family members who help maintain and nurture the patients' social connections. The fact that these family members make possible their participation in our research supports this idea. Indeed, patients with focal hippocampal damage have social networks that are composed of a higher percentage of family members than their non-amnesic counterparts. In the case of the patients with combined hippocampal and amygdala damage, 100% of their social network is composed of nuclear family. In the present study, we didn't differentiate between pre-morbid relationships and relationships acquired after brain damage. It may be that the patients with focal damage to the hippocampus have been able to maintain their pre-morbid relationships more easily than patients with amygdala damage due to support from their family because of their memory impairment (Rosenbaum et al., 2005). For example, the individuals with focal amygdala damage had social networks comprised of a significantly smaller proportion of nuclear family in their social network (20%). While it is difficult to determine the specific factors that lead to the differences in the composition of the social networks, it is an area of future research that is warranted.

In taking a closer look at the people who made up the patients' social networks, it was found that Patient 46 reported her close others to include individuals who were in the role of a nurse or counselor. Furthermore, the third person she listed served in the capacity of a researcher studying how their type of brain damage impacted cognitive and emotional functions. In contrast, Patient 2405 reported her close others as consisting of two friends (one from childhood) and a cousin. In neither case did the patient report someone from their immediate family as a close other, which is distinct from the patients with hippocampal damage. It is possible that family members may have an easier time "connecting" with a patient who has a memory impairment but is otherwise socially intact, than one who has more difficulties with social interaction (as in the case of amygdala damage) marked by difficulties displaying empathy, detecting the emotions of others, and building and maintaining social relationships.

We also examined whether the types of relationships the patients had related to the developmental nature or sudden onset of their lesions. For the two patients with focal damage to the amygdala, the cause was developmental (i.e., Urbach Wiethe disease), whereas for the two patients with damage to the hippocampus and amygdala, it involved a sudden onset due to HSE in adulthood. Despite the differences in lesion onset, in both

cases, the patients had few people in their social network. Yet, the patients with hippocampal and amygdala damage reported their close others as being from their immediate family, whereas the patients with focal amygdala damage did not. Similarly, the patients with focal damage to the hippocampus also reported close others as being from their immediate family (in addition to friends). Davidson and colleagues also reported that developmental amnesic patient HC had relatively normal social functioning (Davidson et al., 2012). Taken together, this provides preliminary evidence that lesion location (i.e., hippocampal or amygdala) rather than time of onset may help to explain differences in social functioning.

The current study extends previous work on social network size by assessing social network size, loneliness, and life satisfaction in the same study. We found that in the group of three patients with amygdala damage (for whom we had data), whether restricted to or combined with hippocampal damage, two out of three reported loneliness scores within the highly lonely range, as well as low levels of life satisfaction. Patient 46, who has focal amygdala damage, and patient 1951, who has both amygdala and hippocampal damage, reported high levels of loneliness and lower levels of life satisfaction. Patient 2308, who also has both amygdala and hippocampal damage, had a loneliness score within the normal range and reported high life satisfaction. Nonetheless, like social network size, damage to the amygdala, on average, may be more associated with higher risks for loneliness and poor life satisfaction. That the patients with hippocampal damage had loneliness and life satisfaction scores similar to that of the healthy comparison group is in contrast to descriptions of such patients as, “stuck in the moment,” (Corkin, 1984, although see, Craver et al., 2014; Kwan et al., 2012), or being socially isolated. While profound memory impairment is certainly a risk factor for a loss of social participation opportunities, as discussed above, it is not the uniform outcome for all memory impaired patients. Rather, it is possible to stay socially connected and feel high levels of life satisfaction despite memory impairment, especially with family support.

The current study also expands on previous work through the incorporation of informant ratings. One limitation of the study was the use of questionnaire measures to assess loneliness and social networks, which may be affected by social desirability bias. Furthermore, individuals with damage to the hippocampus have memory impairments that may affect their capacity for reliable self-reports. Our motivation in obtaining informant data was to check the veracity of the information obtained from participants with deficits in recalling their daily experiences who might under- or over-report the number of individuals in their network. While patients and family members, in general, had high agreement in the number of individuals that constitute their social network, their ratings of perceived life satisfaction and loneliness of their family members was revealing. Family members of patients with hippocampal damage rated their loved ones has having higher perceived loneliness (M=45.8; highly lonely cut-off=45) than reported by the patients (M=37.5). Six out of 7 patients with hippocampal damage reported life satisfaction levels in the moderate to high range (with 1 patient reporting low satisfaction). Strikingly, the informants consistently rated the patients as having low satisfaction. The similarity, or lack thereof, in such ratings between neurological patients and their family members and caregivers is important information for family counseling and for promoting mental health and well-being in these populations. It is also possible that family members are projecting their own feelings

onto the patients, and their ratings may not accurately reflect how the patient actually feels. Future work should assess the stability of such ratings in patients and family members over time.

Limitations of the present study include the comparison of individuals with developmental and adult-onset lesions, and variation in lesion size across the groups. Patients with amygdala damage had a lesion onset around 10 years of age, whereas the other two patient groups incurred lesions in adulthood (on average 36 years of age and older). This difference in age of lesion onset has implications for social development in general, and for social network size. It is interesting to note, however, that both groups of patients with amygdala damage have similar social network sizes and those social networks are markedly smaller than the group of patients with focal hippocampal damage. Anecdotally, the family members of patient 1951 and 2308, who have amygdala and hippocampal damage, report a shrinking social network as these patients lost friends and romantic partners after their brain injuries and were largely unable to develop new meaningful relationships. This may suggest that amygdala damage disrupts both the development and maintenance of social relationships. Furthermore, as noted above Davidson and colleagues (2012) reported that developmental amnesia patient HC had relatively normal social functioning. We note that lesion size varied across the groups. The patients with damage to the amygdala and hippocampus have much larger lesions than the patient groups with focal damage to either the hippocampus or the amygdala. In addition to lesion location, it is possible that lesion size impacts social functioning. Future studies that compare social network size in larger groups of patients with damage to the hippocampus and/or amygdala of varying lesion size as a result of both early onset and late onset lesions are warranted.

Future research is needed to replicate our findings on the amgydala and hippocampus and to understand the role of the full neural network underlying social cognition and interaction, including the ventromedial prefrontal cortex, insula, and anterior cingulate cortex (Adolphs et al., 2005; Kennedy & Adolphs, 2012; Stanley & Adolphs, 2013) on social network size, loneliness, and life satisfaction. For example, it is well established that the ventromedial prefrontal cortex plays a critical role in social relationships and decision making (Barrash et al., 2000; Abel et al., 2016; Anderson et al.,1999; Anderson et al., 2000). Furthermore, brain damage can also disrupt the white matter connections between social brain regions, as is seen in patients with traumatic brain injury who have also been shown to have difficulties with social interaction and empathy that may impact social relationships (McDonald, 2013; Osborne-Crowley & McDonald, 2016). Such work will elucidate the range of clinical populations at risk for disruptions in social relationships and may play an important role in their clinical management to prevent cascading physical and mental health problems associated with feelings of loneliness and poor life satisfaction. By targeting these patients early on, it may help to prevent later issues that have negative impacts on their health and well-being (Tlustos et al., 2016).

In summary, this study compares the association between amygdala and hippocampal damage and social network size, loneliness, and life satisfaction. We find that damage to the amygdala, whether in the context of focal or broader damage (including the hippocampus), is associated with smaller social networks than in healthy adults. This

provides clear evidence for the critical role the amygdala plays in social network size and increased perceived loneliness. In contrast, patients with focal hippocampal damage show relatively preserved social network sizes and reported levels of loneliness and life satisfaction comparable to those of healthy comparison participants. Future research may tease apart the complex interactions between how social network size is impacted by the location of brain damage, the role of family members in the patients' social lives, and how these factors change over the course of recovery and time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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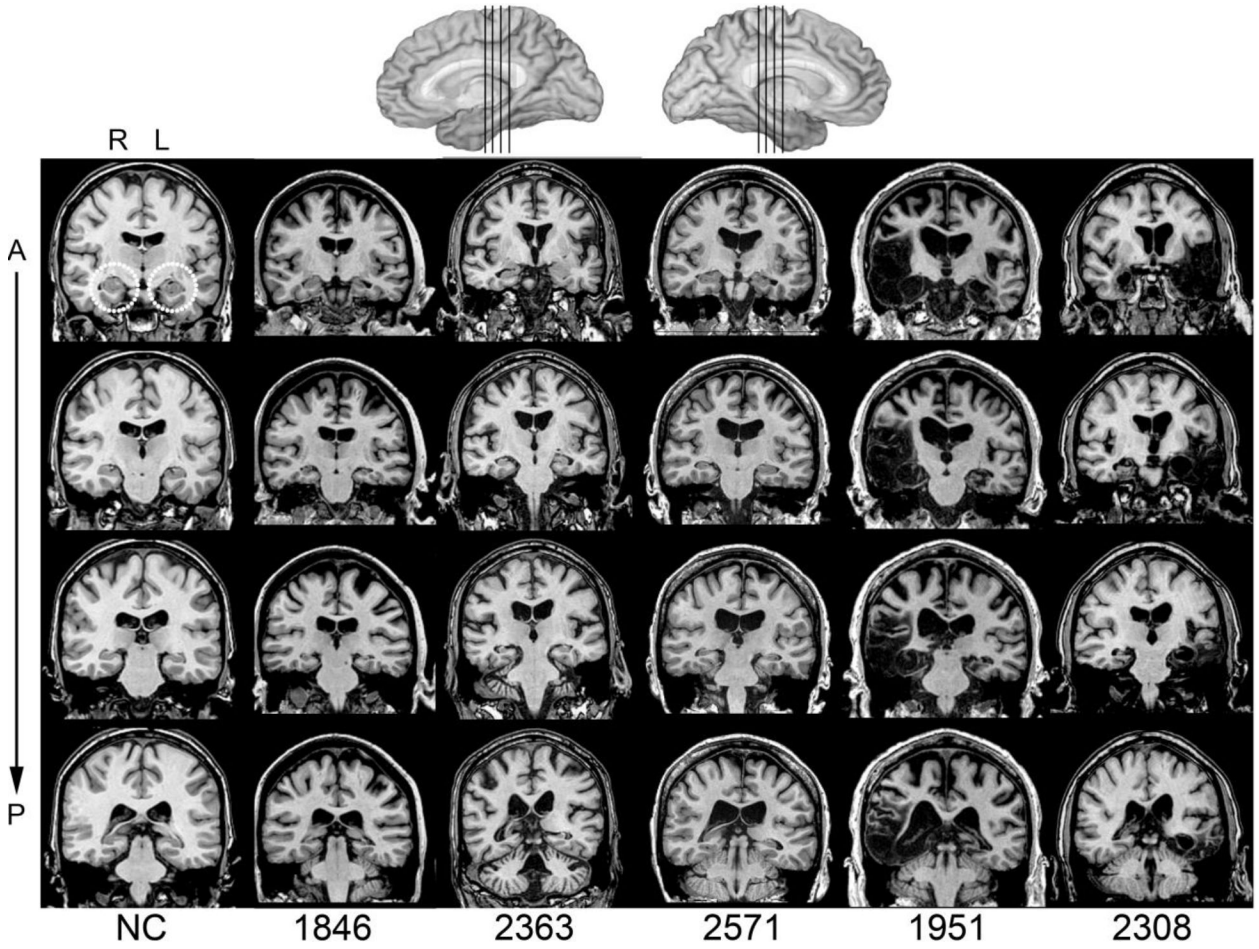
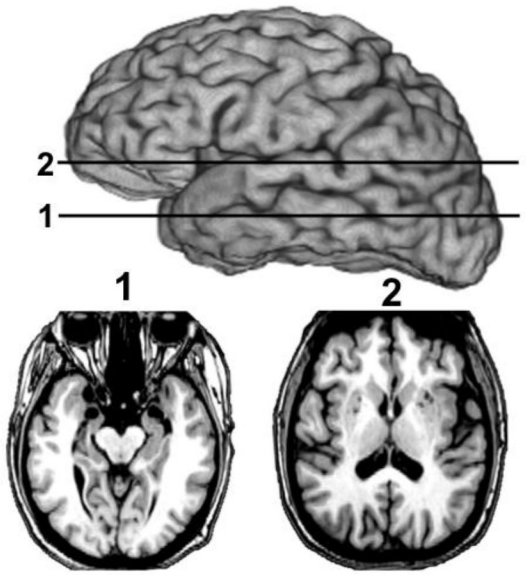


Figure 1.

Image represents high resolution structural magnetic resonance image for patients with damage to the hippocampus (including patients: 1846, 2363, 2571) and patients with damage to the hippocampus and amygdala (including patients: 1951, and 2038). R = right; L = left; A = anterior; P = Posterior; NC = non-injured comparison brain.

A. 46



B. 2405

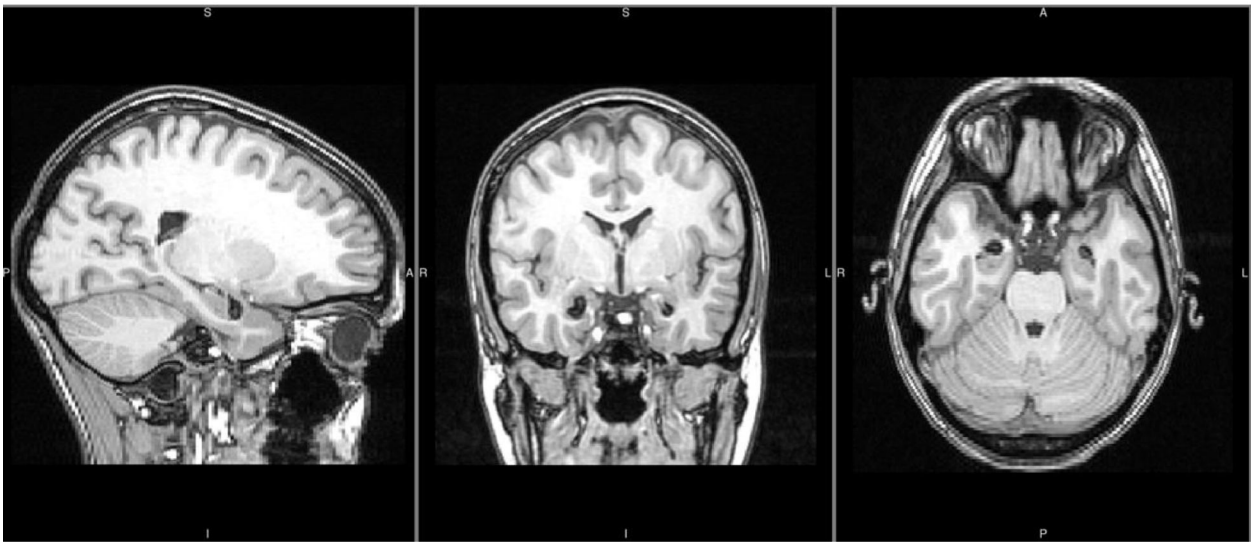


Figure 2.

A. Image depicts high resolution magnetic resonance image of patient with amygdala damage (patient 46) (adapted from Feinstein et al., 2011). B. Image depicts high resolution magnetic resonance image of patient with amygdala damage (patient 2405).

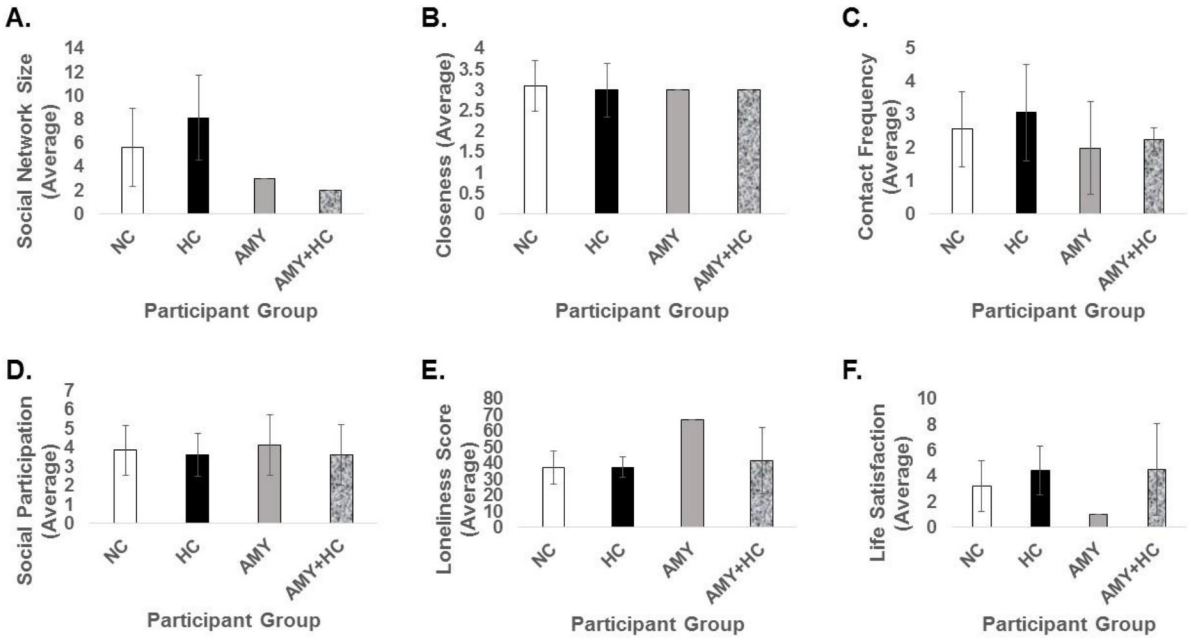
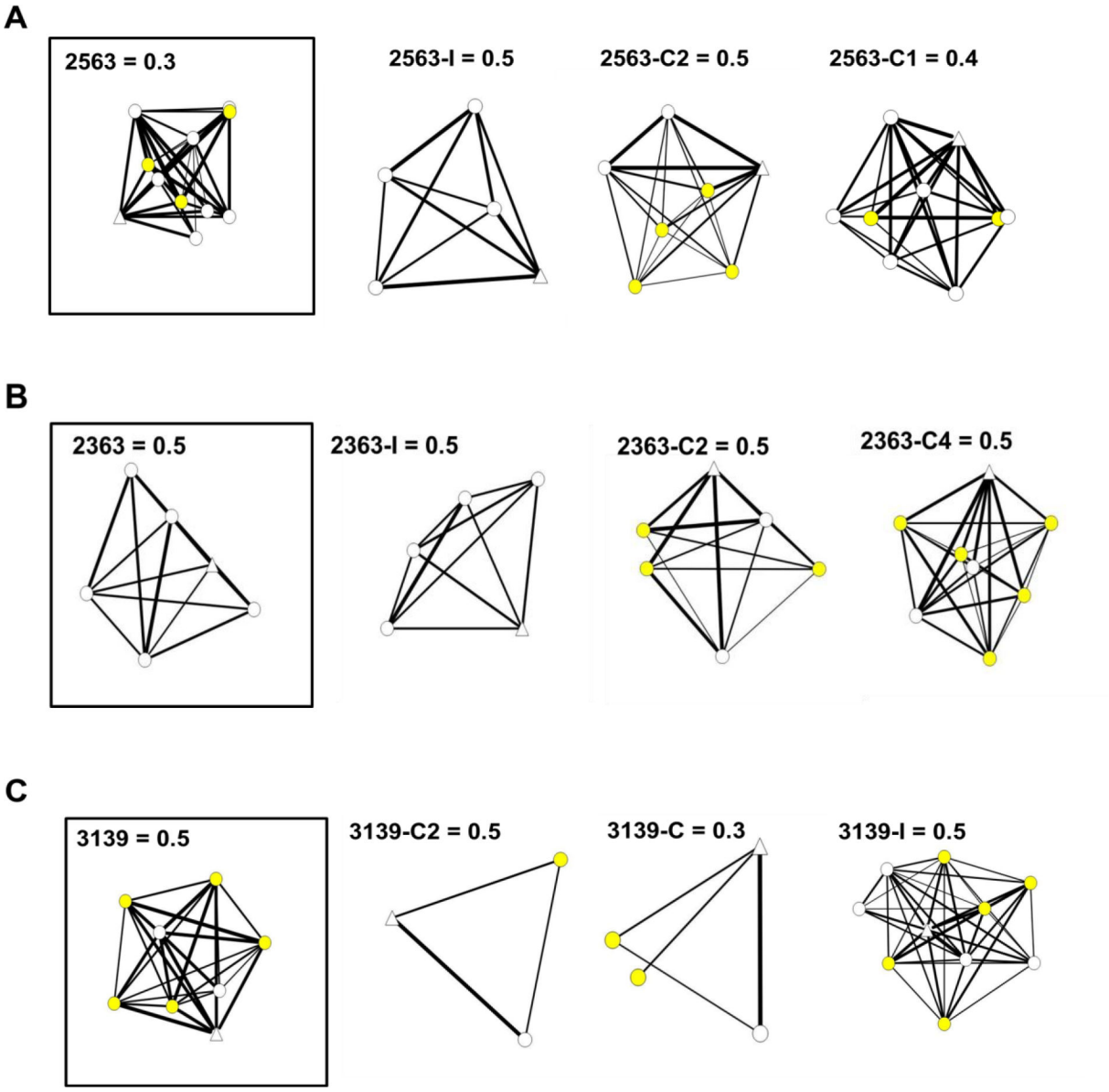
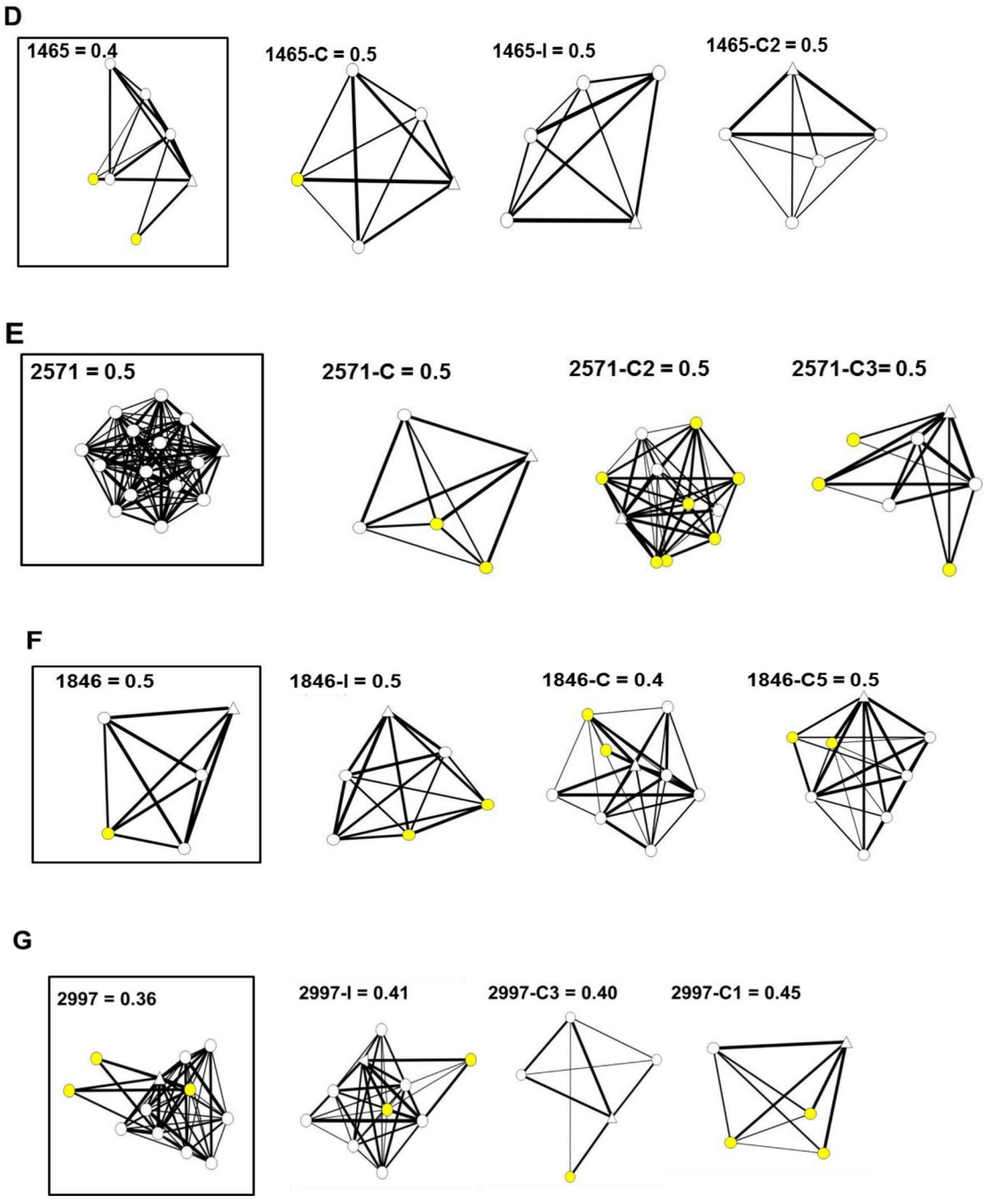


Figure 3.

Panel graph represents average scores of each group on the six main parameters of interest. Error bars indicate standard deviation. NC=non-injured, healthy comparison group. HC=patients with focal damage to the hippocampus. AMY=patients with focal, amygdala lesions. AMY+HC=patients with damage to the hippocampus and amygdala. A. Average social networks size per group. B. Average closeness per group. C. Average contact frequency per group. D. Average social participation per group. E. Average loneliness per group. F. Average life satisfaction per group. Total friends (i.e., social network size), social participation, closeness, and frequency of contact are scores drawn from the NSHAP questionnaire. Loneliness was measured by the UCLA Loneliness Scale and reflects the individual patients' sum scores. Life satisfaction was assessed by the Life Satisfaction Index A and the patients' sum scores on the scale. In some cases, only 1 patient out of the group was available to complete a specific measure. Please note that in some cases two of the patients within a patient group of two had the same response, and thus in this case the standard deviation would be 0.





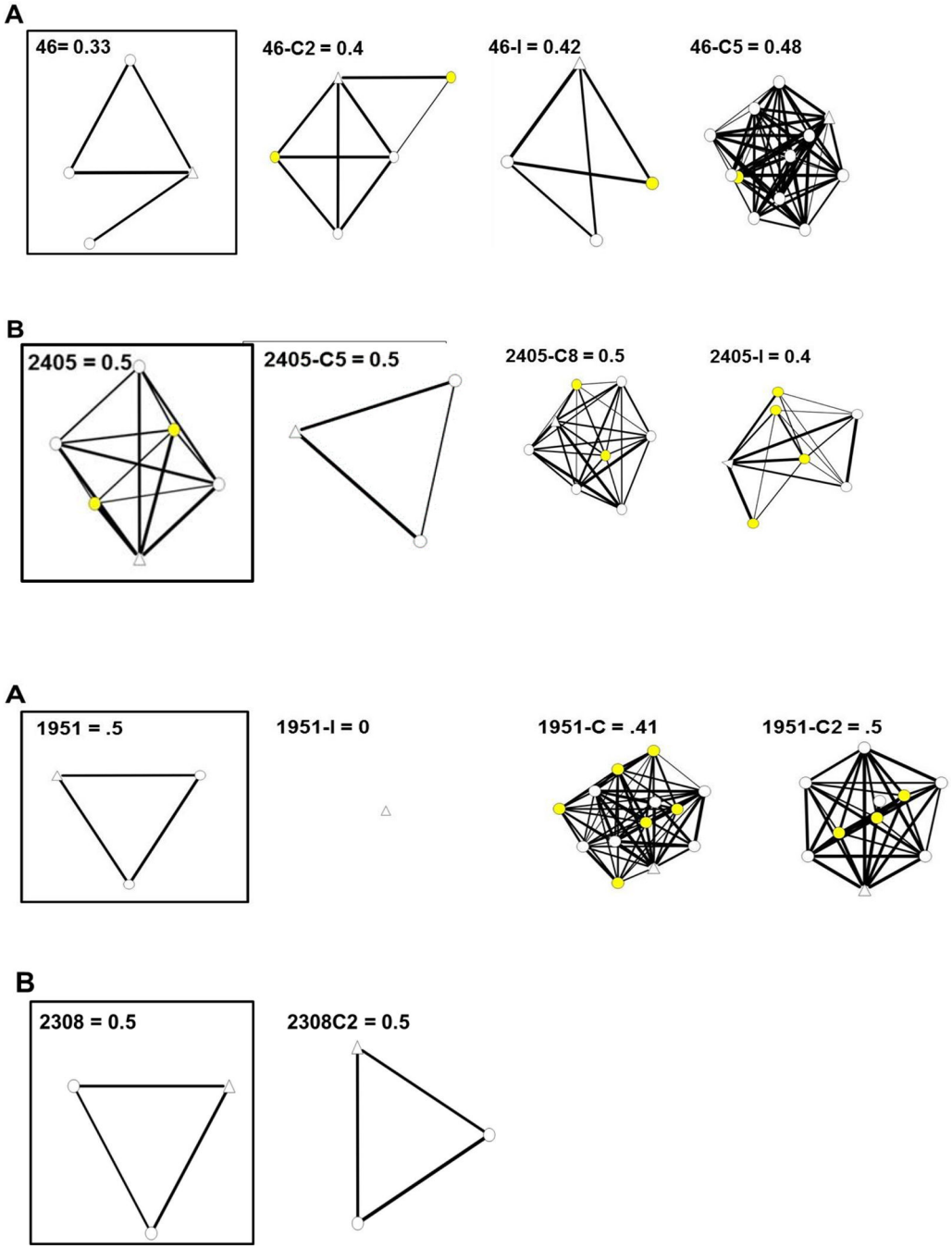


Figure 4.

Individual density maps for each patient are depicted by group. Part 1 includes patients with focal damage to the hippocampus—Part A (Patient 2563), Part B (Patient 2363), Part C (Patient 3139), Part D (Patient 1465), Part E (Patient 2571), Part F (Patient 1846), and Part G (Patient 2997). Part 2 lists patients with focal damage to the amygdala—Part A (Patient 46), and Part B (Patient 2405). Part 3 includes patients with damage to the hippocampus and amygdala—Part A (Patient 1951) and Part B (Patient 2308). The patient is identified with their participant ID number and the bolded square. The family member informant ratings

of the patient include the density map depicted with an I after the patient ID. Examples of comparison participants matched to each patient are identified with the patient ID followed by Part C. Density maps are listed in order of the number of connections. The density value for each participant is listed after the participant ID. Density values range from 0 - .5, with the highest possible value being .5. The more lines there are between each of the nodes in the network indicates that the network is denser, meaning that more of the individuals interact with each other. The triangle shape stands for the participant; the circles indicate a family member of the participant; and the circles in yellow indicate that it is a friend rather than a family member. The lines indicate that a particular individual in the network speaks with another individual in the network. A thicker line shows that the linked individuals speak more often.

Table 1

Participant Demographic Information.

	HC N=7	AMY N=2	AMY+HC N=2	NC N=102
	M (SD)	M (SD)	M (SD)	M (SD)
Age, yrs.	61.6 (11.3)	39.5 (13.4)	60.0 (2.8)	54.5 (13.2)
Education, yrs.	16.0 (2.3)	14.0 (2.8)	17.0 (1.4)	16.0 (1.9)
Sex	5M, 2F	2F	2M	43M, 59F
Lesion Onset Age, yrs.	46.0 (10.7)	10 (0)	35.5 (10.6)	NA
Chronicity, yrs.	16.7 (5.2)	29.50 (13.4)	25.5 (13.4)	NA
Handedness	6R	2R	1R	94R
Marital Status (married/not married)	6/1	0/2	0/2	68/34

Note. HC= patients with damage to the hippocampus. AMY=patients with bilateral amygdala damage due to Urbach Wiethe disease. AMY+HC=patients with amygdala damage due to herpes simplex encephalitis; includes damage to certain regions in the hippocampus. NC=non-injured comparison participants. Yrs.= years. M=male, F=female. R=right-handed, L=left-handed. Marital status=Indicates proportion of participants who are married versus not married.

Table 2.

Neuropsychological Characterization of Patients.

	WAIS-III FSIQ	WAIS-III WMI	WMS-GMI	Boston Naming	Token test	BDI
HC (N=7)						
2563	94	88	63	57	44	0
2363	98	90	73	58	44	0
1846	84	90	57	43	41	9
3139	107	99	78	60	43	8
1465	110	88	79	57	43	8
2997	112	104	N/A	57	44	8
2571	112	99	87	59	44	2
AVG (SD)	102.4 (10.7)	94.0 (6.5)	72.8 (11.1)	55.9 (5.8)	43.3 (1.1)	5.0 (4.1)
AMY (N=2)						
46	80	N/A	124	N 49	44	12
2405	98	86	N/A	46	N/A	N/A
AVG (SD)	89.0 (12.7)	86	124	47.5 (2.1)	44	12
AMY+HC (N=2)						
2308	98	86	45	52	44	0
1951	106	94	57	49	44	5
AVG (SD)	102.0 (5.7)	90.0 (5.7)	51.0 (8.5)	50.5 (2.1)	44.0 (0)	2.5 (3.5)
Statistic *p*-value	0.33	0.24	0.89	0.05	0.31	0.84

Note. HC= patients with damage to the hippocampus. AMY=patients with bilateral amygdala damage due to Urbach Wiethe disease. AMY+HC=patients with amygdala damage due to herpes simplex encephalitis; includes damage to certain regions in the hippocampus. WAIS-III=Wechsler Adult Intelligence Scale Version Three. Subscales: FSIQ=Full scale intelligence quotient; WMI=Working Memory Index. WMS-GMI=Wechsler Memory Scale-General Memory Index. BDI= Beck Depression Inventory. AVG=average. SD=standard deviation.

Table 3

Social Network Characteristics

	Total Friends	Social Participation	Closeness	Freq Contact	Loneliness	Life Satisfaction
HC (N=7)						
2563 (M)	10	3.75	3	2	39	5
2363 (M)	5	4	2	5	44	5
3139 (M)	7	2	3.5	1.5	28	5
1465 (M)	5	2.5	3	3	40	7
2997 (M)	11	5.25	4	4	40	1
1846 (F)	5	4.5	3	1.5	43	3
2571 (F)	14	3.25	2.5	4.5	29	5
AVG (SD)	8.14 (3.58)	3.61 (1.13)	3.00 (0.65)	3.07 (1.46)	37.57 (6.45)	4.43 (1.90)
AMY (N=2)						
46 (F)	3	3	3	3	67	1
2405 (F)	3	5.25	3	1	N/A	N/A
AVG (SD)	3.00 (0)	4.13 (1.59)	3.00 (0)	2.00 (1.41)	67	1
AMY+HC (N=2)						
2308 (M)	2	2.5	3	2.5	27	7
1951 (M)	2	4.75	3	2	56	2
AVG	2.00 (0)	3.63 (1.59)	3.00 (0)	2.25 (0.35)	41.50 (20.51)	4.50 (3.54)
NC (N=102)						
AVG (SD)	5.62 (3.30)	3.86 (1.31)	3.09 (0.61)	2.57 (1.13)	37.32 (10.28)	3.21 (1.95)
NC (N=43; Males)						
AVG (SD)	4.86 (2.60)	3.84 (1.47)	2.95 (0.59)	2.93 (1.15)	38.58 (9.00)	3.08 (1.90)
NC (N=59; Females)						
AVG	6.17 (3.66)	3.88 (1.19)	3.19 (0.60)	2.30 (1.05)	36.33 (11.18)	3.31 (2.01)

Note. HC=patients with focal damage to the hippocampus. AMY=patients with focal, amygdala lesions. AMY+HC=patients with damage to the hippocampus and amygdala. NC=non-injured, healthy comparison group. AVG= average score of the group. SD=standard deviation. Total friends, social participation, closeness, and frequency of contact are scores drawn from the NSHAP questionnaire. Loneliness was measured by the UCLA Loneliness Scale and reflects the individual patients' sum scores. Life satisfaction was assessed by the Life Satisfaction Index A and the patients' sum scores on the scale. M=male. F=female.