Northumbria Research Link

Wakeful Rest Promotes the Integration of Spatial Memories into Accurate Cognitive Maps

Michael Craig [1,2], Michaela Dewar [1,2,3], Mathew A. Harris [2], Sergio Della Sala [1,2], Thomas Wolbers [4,5]

[1] Human Cognitive Neuroscience, Department of Psychology, The University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, United Kingdom; [2] Centre for Cognitive Ageing and Cognitive Epidemiology, The University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, United Kingdom; [3] Department of Psychology, School of Life Sciences, Heriot-Watt University, Edinburgh, EH14 4AS, United Kingdom; [4] Aging and Cognition Research Group, German Center for Neurodegenerative Diseases (DZNE), D-39120 Magdeburg, Germany; [5] Center for Behavioral Brain Sciences, D-39118 Magdeburg, Germany

The manuscript contains 27 pages, 4 Figures and 1 Table

Corresponding author: Mr Michael Craig, Human Cognitive Neuroscience, Department of Psychology, The University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ, United Kingdom. Email: M.Craig-4@sms.ed.ac.uk. Phone: +44(0)131 650 2968

Abstract

Flexible spatial navigation, e.g. the ability to take novel shortcuts, is contingent upon accurate mental representations of environments – cognitive maps. These cognitive maps critically depend on hippocampal place cells. In rodents, place cells replay recently travelled routes, especially during periods of behavioural inactivity (sleep/wakeful rest). This neural replay is hypothesised to promote not only the consolidation of specific experiences, but also their wider integration, e.g. into accurate cognitive maps. In humans, rest promotes the consolidation of specific experiences, but the effect of rest on the wider integration of memories remained unknown. In the present study, we examined the hypothesis that cognitive map formation is supported by rest-related integration of new spatial memories. We predicted that if wakeful rest supports cognitive map formation, then rest should boost knowledge of overarching spatial relations that were never experienced directly during recent navigation. Forty young participants learned a route through a virtual environment before either resting wakefully or engaging in an unrelated perceptual task for 10 minutes. Participants in the wakeful rest condition performed more accurately in a delayed cognitive map test, requiring the pointing to landmarks from a range of locations. Importantly, the benefit of rest could not be explained by active rehearsal, but can be attributed to the promotion of consolidation-related activity. These findings (i) resonate with the demonstration of hippocampal replay in rodents, and (ii) provide the first evidence that wakeful rest can improve the integration of new spatial memories in humans, a function that has, hitherto, been associated with sleep.

INTRODUCTION

When visiting a new city we often find it difficult to orientate ourselves initially. However, after a period of exploration we begin to understand the spatial structure of the environment. For example, after travelling from our hotel to an art gallery and then from the art gallery to a science museum, we can gauge the general direction of our hotel from the science museum, thus allowing us to return to our hotel more directly, even though we never experienced this 'shortcut' previously. We owe our ability to navigate flexibly to the automatic formation (Montello, 1998; Ishikawa and Montello, 2006) of a 'cognitive map' (Tolman, 1948). A cognitive map is a flexible mental representation of the spatial relationships (i.e. directions and distances) between objects in the world that can be accessed from any perspective and vantage point (Wolbers and Hegarty, 2010). In contrast to other, more rigid forms of spatial knowledge such as memory for a specific spatial experience (e.g. a travelled route), cognitive maps represent an overarching relational memory built via the *integration* of a number of memories pertaining to the spatial experience. In the research reported here we examined this integration of new memories into a cognitive map. Specifically, we asked whether this integration benefits from a period of post-navigation wakeful rest.

Our research was motivated by compelling recent findings in animal neuroscience and cognitive psychology: in rodents, the navigation of a novel environment is associated with the firing of hippocampal place cells which code for the animal's location (O'Keefe et al., 1998; Moser et al., 2008). During post-navigation periods of relative inactivity (slow wave sleep and wakeful rest), the same cells re-express firing sequences corresponding to specific recent spatial experience, i.e. the earlier travelled route is '*replayed*' (Jackson et al., 2006; Davidson et al., 2009; Karlsson and Frank, 2009). These cells also express *reverse* firing sequences (Foster and Wilson, 2006) and firing sequences that relate to trajectories within the

environment that were *never experienced* (Gupta et al., 2010). These patterns of hippocampal reactivation are hypothesised to support the consolidation of recently travelled routes within memory *and* the wider consolidation and integration of these new spatial memories into accurate cognitive maps (Derdikman and Moser, 2010; Gupta et al., 2010; Carr et al., 2011; Csicsvari and Dupret, 2014).

In humans, research on memory and rest has been confined to memories of *specific* recent experience. This research shows that words and short stories are retained better for at least 7 days if their learning is followed immediately by a few minutes of wakeful rest rather than by novel sensory stimulation (Dewar et al., 2007, 2012a; Craig et al., 2014). In addition, post-learning rest also boosts the long-term retention of spatial associative and temporal order information (Craig et al., 2015). It is hypothesised that wakeful rest promotes early cellular consolidation of such experiences because of the minimal amount of new sensory information and associated encoding, which would otherwise hamper consolidation processes (Mednick et al., 2011; Dewar et al., 2012b, 2014; Craig et al., 2015). Neuroimaging work in humans strengthens this consolidation hypothesis, demonstrating (i) reactivation of recent *specific* encoding-related neural activity (i.e. visual information) during wakeful rest, and (ii) a direct link between the degree of such reactivation and performance on subsequent memory measures (Tambini et al., 2010; Deuker et al., 2013).

Is the rest-related improvement in humans confined to memories of *specific* experiences, or could rest in fact also promote the *wider integration* of such memories within long term memory? The process of memory integration has, hitherto, been assumed to be a function of systems consolidation during human *sleep* (Ferrara et al., 2008; Wamsley et al., 2010; Coutanche et al., 2013; Oudiette et al., 2013). It is possible therefore that the benefit of rest does not extend to memory tasks that assess the wider integration of new memories, such as cognitive map tasks, which examine knowledge of overarching spatial relations that were

never experienced directly during navigation. Using a behavioural cognitive map task, we sought to establish, for the first time, whether or not daytime rest promotes the wider integration of novel memories within long term memory.

To this end, participants first learned a route through a novel virtual town environment and then either rested wakefully or performed an unrelated perceptual task for 10 minutes. Each participant's spatial memory of the earlier experienced environment was then probed, without prior warning, via a cognitive mapping test derived from previous studies (Waller et al., 2004; Wolbers and Büchel, 2005; Ishikawa and Montello, 2006). Given that the hippocampus is widely assumed to support the learning and consolidation of cognitive maps, we predicted the wakeful rest group to outperform the perceptual task group in the accuracy of their cognitive maps.

METHODS

Ethics Statement

This research was approved by the University of Edinburgh's Psychology Research Ethics Committee (Ref: 446-1112). All participants provided their informed consent in writing prior to taking part.

Participants

Forty healthy young adults (19 males, 21 females; mean age = 20.48 years, SD = 1.86) were recruited as participants. All participants had normal or corrected-to-normal vision.

Design

We employed a between-subjects design with two delay conditions (Figure 1). The experiment took place in a single session, divided into a learning phase, a delay phase, and a testing phase. Learning and testing phases were the same for all participants. The critical between-subject manipulation occurred during the 10-minute delay phase, during which participants either: (i) rested wakefully, or (ii) performed an unrelated perceptual task (a spot-the-difference game). During the subsequent testing phase, participants performed a cognitive map test assessing the accuracy of a newly formed cognitive map of the environment navigated during the previous learning phase. The critical measure of the cognitive map test was the accuracy of responses, i.e. the number of degrees of absolute error between the correct direction of the target landmark within the environment and the estimated direction of the target landmark. However, we also recorded the time to initiate a response and the total time to respond since (i) the time taken to respond in memory tests has been suggested to be indicative of the confidence of memory retrieval and memory availability (Gimbel and Brewer, 2011), and (ii) a correlation between response time and distance travelled could suggest that participants solved the pointing task via mental travel (Wolbers et al. 2004; Ghaem et al., 1997) rather than by directly accessing landmark-to-landmark relationships.

<<INSERT FIGURE 1 ABOUT HERE>>

Materials

The virtual environment was created with Autodesk 3ds Max 2012 (copyright Autodesk Inc., San Rafael, CA, USA), by modifying an existing environment (Harris & Wolbers, 2014). The paradigm was run in Vizard 4.0 (copyright WorldViz LLC, Santa Barbara, CA, USA) via a

Python-coded script. The complex environment was a large realistic town-like space comprising a network of roads, non-specific houses, and nine distinctive landmarks. All landmarks were common real-world buildings that would be found in a town-like environment, e.g. a bar, a supermarket and a church (Figure 2). The environment incorporated four 'regions', each of which contained houses of a different style and size. The network of roads connected all of these regions, and at each junction (i.e. decision point) there was a different distinctive landmark. The environment was presented to participants on a 22-inch widescreen monitor. A computer gaming steering wheel (Thrustmaster Ferrari Challenge) was used to input responses during learning and testing.

<<INSERT FIGURE 2 ABOUT HERE>>

Procedure

Learning phase. Participants were told that they would be a 'passenger' in a car travelling through a virtual town. They were informed that they would be required to learn a long, indirect route through the environment and would be asked to provide directions to the experimenter (the 'driver') during a subsequent trial. Route learning was broken into learning cycles; each learning cycle included two learning trials followed by one probe trial. In a learning trial, the participant travelled the trained route (total distance = 480.00 metres) via automated movement (linear movement = 3.50 metres per second, rotation movement = 15 degrees per second, total travel time = 142 seconds), as would a passenger in a car. In a probe trial, the participant again travelled the route. However, on this occasion the automated movement paused at each junction (i.e. decision point) and the participant was asked to state

the direction (i.e. "left", "right", or "straight on") in which the trained route continued from that point. If any errors were made during a probe trial, the participant was required to perform additional learning cycles until the route was learned to a criterion of 100% accuracy, i.e. zero errors. A minimum of two learning cycles (four learning trials and two probe trials) was used to promote learning of the route and reduce the possibility of successful navigation due to chance. Upon successful learning of the route, participants entered the delay phase.

Delay phase. During the 10-min delay phase, participants either (i) rested wakefully or (ii) performed an unrelated perceptual task (a spot-the-difference game). Twenty participants were allocated pseudo-randomly to each delay condition.

Participants assigned to the *wakeful rest* condition were asked to sit quietly in the dimly-lit testing room and relax while the experimenter left the room to "set up the next section of the experiment" (Dewar et al., 2007, 2012a; Craig et al., 2014). Care was taken to ensure that the testing room was devoid of any rich visual and/or audible sensory cues so as to minimise sensory information, and thus the disruption of consolidation. Participants assigned to the *perceptual task* condition were asked to play a visual spot the difference game (Dewar et al., 2012a; Craig et al., 2014). Participants performed 20 spot the difference trials in silence, each 30 seconds in duration. A trial consisted of the presentation of a pair of real-world photos on a 17-inch laptop computer screen. Photo pairs were identical other than for two discrete differences. Participants were instructed to search for differences between photos in a pair, and to point out any discovered differences to the experimenter.

Testing phase. Following the completion of the delay phase, participants performed a cognitive map test, which was based on pointing tasks used in previous studies on cognitive mapping in real and virtual environments (Waller et al., 2004; Ishikawa and Montello, 2006; Weisberg et al., 2014). In this test, participants were required to indicate spatial relationships

between the nine landmarks encountered previously along the learned route. Participants performed 16 trials, presented in a random order across all participants. As with learning, this test was presented on a 22-inch monitor. In each trial, the participant was positioned facing one of the nine landmarks within the environment. They were then instructed on-screen to rotate to face towards a second, specified target landmark within the environment. The speed of rotation was 15 degrees per second, and the mean angle to be rotated between the starting orientation and direction of the target landmark across the 16 cognitive map trials was 120 degrees. To ensure that our test indeed probed knowledge of overarching spatial relations that had *never been experienced directly*, the target landmark never represented the landmark that had followed on immediately from the participant's current position during earlier route learning. Moreover, the target landmark was never visible from the participant's current position, and hence accurate pointing performance depended on their metric and configural knowledge of the environment. For example, Figure 2 shows a test trial in which the participant was positioned facing the church and instructed to turn to face towards the Chinese restaurant (target landmark). A white crosshair (see Figure 2) appeared in the centre of the screen to ensure that an accurate response could be obtained. Responses were inputted by the participant via the same steering wheel as used during learning. Participants rotated within the environment via the 'left' and 'right' directional keys until the central white crosshair was in line with the direction they believed the target landmark to be. Participants then confirmed their response via pressing the 'up' directional key on the steering wheel.

Upon completion of the cognitive map test, participants completed the Santa Barbara Sense of Direction (SBSOD) questionnaire (Hegarty et al., 2002), as well as a detailed post-experimental questionnaire in which they were asked: (i) whether they had expected a further memory test, and (ii) whether they had thought about the virtual environment, learned route, landmarks and/or any other associated features during the 10-min delay. If intentional thoughts

were reported, participants were asked a follow-up question of whether any information was actively rehearsed during the delay. Ratings of past experience using computers, playing video games and using virtual reality software were also collected (Moffat et al., 2001).

Scoring

The cognitive map test was scored by calculating, for each trial, the absolute deviation (in degrees) between the correct direction of the target landmark and the participant's estimated direction of the target landmark (see Figure 2). The mean pointing error score was then calculated for each participant by averaging the pointing errors across the 16 trials. Group means were computed subsequently.

Statistical analyses

Inferential analyses were performed using SPSS Statistics 19 (copyright IBM Corp., NY, USA), with the alpha level set to .05. Bayesian analyses were performed using JASP (version 0.6.6) (Love et al., 2015). ANOVAs with between-subject factor delay condition (wakeful rest vs. perceptual task) were performed to examine group differences in learning and cognitive map test performance. ANCOVAs were run with covariates 'gender', 'self-reported sense of direction (SBSOD)' and 'past experience using computers' in order to examine group differences in learning and cognitive map performance, after controlling for the effects of these variables. Pearson correlations were performed to examine the relationship between accuracy and response time in the cognitive map test. Lastly, in order to examine if the cognitive map test might have been solved via mental travel along the route rather than direct access to landmark-to-landmark relationships, Pearson correlations were run for each participant (i) between absolute pointing error (degrees) and the distance travelled previously between the presented landmark and the target landmark, and (ii) between response initiation and total response time and the distance travelled previously between the presented landmark and the

target landmark. These correlation coefficients were normalized using Fisher's r-to-z transformation and subsequently compared to 0 (no correlation) via Bayesian one-sample t-tests, for the two delay condition groups separately. As we did not have previous data to base prior assumptions, the default Cauchy(0,1) prior for effect size ($\sigma = 0.707$) was used (Rouder et al., 2009).

RESULTS

The wakeful rest group and the perceptual task group did not differ significantly in gender ratio (wakeful rest: 11 females, 9 males; perceptual task: 10 females, 10 males, $p = 1.000$, Fisher's exact test), age ($F(1,38) = 0.88$, $p = .355$, $\eta\rho^2 = .023$), experience with computers ($F(1,38) = 0.73$, $p = .397$, $\eta\rho^2 = .019$) or self-reported sense of direction ($F(1,38) = 0.12$, $p = .729$, $\eta\rho^2 = .003$).

Route learning

Learning cycles. All but one participant (wakeful rest group) were able to learn the route to a 100% criterion within the fixed minimum of two learning cycles (four learning trials and two probe trials). The participant who did not learn the route within two learning cycles was able to do so within three learning cycles. This did not produce a significant main effect of group on the number of learning cycles required to learn the route ($F(1,38) = 1.00$, $p = .324$, $\eta\rho^2 = .026$). This finding did not change after controlling for the effects of gender, self-reported sense of direction, and past experience with computers ($F(1,35) = 0.98$, $p = .330$, $\eta\rho^2 = .027$). No covariates were significantly related to the number of learning trials required (all $p > .288$).

Learning errors. Table 1 shows the mean number of errors made by the two groups during each route learning probe trial individually, as well as during learning overall. There was no main effect of group on the number of errors made during route learning ($F(1,38) = 0.15$, $p = .699$, $\eta\rho^2 = .004$). This finding did not change after controlling for the effects of gender, self-reported sense of direction, and past experience with computers ($F(1,35) = 0.08$, $p = .778$, $\eta\rho^2 = .002$). No covariates were significantly related to the number of errors made during learning (all $p > .640$). Taken together, these analyses show that the two groups did not differ significantly in terms of route memory performance prior to the critical delay (wakeful rest vs. perceptual task).

<<INSERT TABLE 1 ABOUT HERE>>

Cognitive map test

Accuracy of responses. Figure 3 shows the two groups' accuracy of responses, i.e. the mean angle of absolute pointing error, in the cognitive map test. There was a significant main effect of group on the accuracy of responses in the cognitive map test ($F(1,38) = 8.94$, $p = .005$, $\eta\rho^2 = .190$), such that the wakeful rest group outperformed the perceptual task group. This benefit of wakeful rest remained after controlling for the effects of gender, self-reported sense of direction (SBSOD), and past experience with computers ($F(1,35) = 9.54$, $p = .004$, $\eta\rho^2 = .214$). No covariates were significantly related to the mean angle of absolute pointing error (all $p > .389$).

<<INSERT FIGURE 3 ABOUT HERE>>

The mean pointing error (averaged over 16 trials) was below chance (90 degrees of error) for all participants. However, three participants in the wakeful rest group and six participants in the perceptual task group did provide responses in one or more trials which were above chance. When a threshold of 90 degrees of error (i.e. chance) was imposed on the data, and any responses above this threshold were removed, the significant benefit of wakeful rest remained ($F(1,38) = 9.913$, $p = .003$, $\eta\rho^2 = .207$). As before, this benefit remained after controlling for the effects of gender, self-reported sense of direction (SBSOD), and past experience with computers ($F(1,35) = 12.745$, $p = .001$, $\eta\rho^2 = .267$). No covariates were significantly related to the mean angle of absolute pointing error (all $p > .114$).

Response times. There was no effect of group on the total time taken to respond to cognitive map test trials (wakeful rest group: mean = 16.94 s, SEM = 0.93; perceptual task group: mean = 15.46 s, SEM = 0.82; $F(1,38) = 1.425$, $p = .240$, $\eta\rho^2 = .036$). This finding did not change after controlling for the effects of gender, self-reported sense of direction, and past experience with computers ($F(1,35) = 1.042$, $p = .314$, $\eta\rho^2 = .029$). No covariates were significantly related to the mean total response time, although the effect of self-reported sense of direction on mean total response time approached significance ($p = .093$). All other p values were > .352. Finally, there was no evidence for speed-accuracy trade-offs in the cognitive map test, because the total time taken to respond was unrelated to the accuracy of responses ($r = .174$, $p = .284$).

There was also no effect of group on the time taken to initiate a response in the cognitive map trials (wakeful rest group: mean = 2.42 s, SEM = 0.07; perceptual task group: mean = 2.53 s, SEM = 0.08; $F(1,38) = 0.058$, $p = .811$, $\eta\rho^2 = .002$). This finding did not change after controlling for the effects of gender, self-reported sense of direction, and past experience with

computers ($F(1,35) = 0.3009$, $p = .582$, $\eta \rho^2 = .009$). No covariates were significantly related to the mean response time (all $p > .368$), and there was no evidence for speed-accuracy trade-offs, as the time taken to initiate a response was unrelated to the accuracy of responses ($r = .069$, $p = .673$).

Instead of directly accessing landmark-to-landmark relationships, participants could have solved the pointing task by mentally travelling along the route from the presented to the target landmark. This strategy would lead to longer response times and larger pointing errors the longer the distance along the route between both landmarks (Wolbers et al., 2004). However, a Bayesian one-sample t-test on Fisher z-transformed r values provided *some* (BF_{01} = odds greater than 3) to *strong* (BF_{01} = odds greater than 10) evidence (Jeffreys, 1961) in favour of the null hypothesis, i.e. that there was no correlation between the distance between landmarks and total response time (wakeful rest: $BF_{01} = 12.518$, perceptual task: $BF_{01} = 11.602$; see also Figure 4), time to initiate a response (wakeful rest: $BF01 = 4.303$, perceptual task: $BF01 = 3.908$), or pointing errors (wakeful rest: $BF_{01} = 3.613$, perceptual task: $BF_{01} = 9.977$). Taken together, these findings suggest that participants did not solve the cognitive map test via mentally travelling along the route.

<<INSERT FIGURE 4 ABOUT HERE>>

Post-experimental reports

As found in previous research (Dewar et al., 2012a; Craig et al., 2014), the majority of participants (n = 13) in the wakeful rest group reported spontaneous mind-wandering during the wakeful rest delay condition, incidentally recalling the past and thinking about the future.

Also, ten participants (50 %) in the wakeful rest group and six participants (30 %) in the perceptual task group reported that they had expected a further memory test at the end of the experiment. All significant effects remained significant when these participants were removed from the analyses. Additionally, five participants (25 %) in the wakeful rest group and one participant (5 %) in the perceptual task group reported that they had intentionally rehearsed information from the learned route during the 10-min delay. None of the results changed when these participants were removed from our analyses.

In the wakeful rest group, in addition to the five participants (25%) who reported active rehearsal, a further five participants (25%) reported spontaneous (i.e. 'popped' into their mind) thoughts pertaining to the learned route during the rest delay. The remaining 10 participants (50 %) reported no intentional/spontaneous thoughts. When those who reported intentional and/or spontaneous thoughts (10/20, 50%) about the route were compared against those who did not (10/20, 50%), no difference was observed in cognitive map test performance ($F(1,18)$ = 1.408, p = .251, $\eta\rho^2$ = .072). Similarly, when the five participants (25 %) in the wakeful rest group who reported rehearsal were compared against those who did not rehearse (15/20, 75 %), no difference was observed in cognitive map test performance ($F(1,18)$ = 0.803, p = .396, $\eta\rho^2$ = .091).

DISCUSSION

When navigating an unfamiliar environment, our memory system automatically forms a flexible mental representation of the spatial relationships (i.e. directions and distances) between objects in the world that are accessible from any perspective and vantage point, i.e. a *cognitive map*. The present results suggest that the *accuracy* of such a newly formed cognitive map can be improved significantly via a post-navigation rest. Participants who rested for 10 minutes

immediately after route learning were able to more accurately estimate the direction of landmarks within the virtual environment than were participants who performed a perceptual task during the same time. These results are in line with rodent findings and suggest that efficient replay of navigational experiences can support the integration of novel spatial information into cognitive maps (Derdikman and Moser, 2010; Gupta et al., 2010; Csicsvari and Dupret, 2014).

The memory benefit in the rest group cannot be accounted for by potential random group differences in pre-delay route memory, gender ratio, past experience with computers, or sense of direction. The two groups did not differ significantly in route learning or final recall *prior* to the critical delay, or in the other variables (gender ratio, past experience with computers, sense of direction). Moreover, the benefit of wakeful rest persisted after controlling for these variables. This indicates that the improvement in cognitive map accuracy was indeed the result of our wakeful rest manipulation.

It is also highly unlikely that this improvement in cognitive map accuracy can be attributed merely to intentional rehearsal of the learned route/landmarks during the rest delay. Although some participants (25 %) in the rest group reported that they intentionally rehearsed aspects of the learned routes, the significant benefit of wakeful rest persisted following their exclusion from analysis. Furthermore, there was no difference in cognitive map test performance between those who rehearsed and those who did not. Moreover, unlike a route recall test, our surprise cognitive map test probed knowledge of overarching spatial relations that were never experienced directly. Therefore, intentional route rehearsal during the delay would have been of limited benefit in the subsequent cognitive map test, unless participants solved this test by mentally traveling along the route. However, this is unlikely for a number of reasons. Firstly, the short time that participants took to initiate a response is unlikely to have provided sufficient opportunity for them to mentally travel the route prior to responding.

Secondly, although total response times were rather long and could suggest that participants mentally travelled the route while responding, they can be explained simply by the limited speed of rotation through the virtual environment (15 degrees per second). Moreover, increased distance along the learned route *did not* lead to increased initiation and/or total response times or pointing errors, which would be expected if participants solved the test via mentally traveling along the route (Wolbers et al., 2004, Ghaem et al., 1997). It could be argued that our correlations between distance travelled and initiation/total response times suffered from issues of range restriction. However, a strong effect of distance in the time taken to mentally travel a learned route has been observed in a range of distances smaller than that used in our study (40m to 140m, Ghaem et al., 1997). Together these findings indicate that (i) participants solved the cognitive map task by directly accessing landmark-to-landmark relationships, rather than by mentally travelling along the route, and (ii) intentional rehearsal is an unlikely account of the rest-related boost in cognitive map accuracy.

These findings bolster related research in verbal memory demonstrating that the rest-induced memory improvement (i) is not dependent upon intentional rehearsal (Dewar et al., 2014), but (ii) is likely to be the result of superior memory consolidation (Dewar et al., 2014). Crucially, the results of the present study suggest that rest periods not only promote the consolidation of specific experiences (e.g. word lists), but also the wider integration of complex memories (e.g. directions between landmarks), resulting in improved memory of never-experienced spatial relations. This finding resonates with the discovery in rodents of rest-associated hippocampal replay of experienced trajectories as well as of trajectories that were *never* travelled during actual exploration (O'Keefe et al., 1998; Davidson et al., 2009; Harvey et al., 2009; Gupta et al., 2010; Wills et al., 2010).

The rest period in our human study could have been conducive to hippocampal replay/consolidation due to the minimal amount of new sensory information and associated

encoding. It has been hypothesised that novel encoding hampers the consolidation of new memories (Craig et al., 2014; Mednick et al., 2011; Dewar et al., 2012). In our perceptual task delay, participants likely encoded a lot of novel sensory information throughout the delay, and this could have interrupted the hippocampal replay of experienced and never experienced relations and trajectories. In contrast, the minimal sensory information during the rest delay probably resulted in reduced novel encoding, and this could have provided superior conditions for hippocampal replay, resulting in higher accuracy in our cognitive map test. It should be noted that some encoding will also take place during rest delays, given that participants typically think about the past and future, resulting in novel encoding. Indeed, when such thoughts are rich in episodic content, they can interfere somewhat with ongoing memory consolidation (Craig et al., 2014), and this might account for individual differences in the degree of rest-related memory improvement (Craig et al., 2014). On the whole, however, we hypothesise that novel encoding during rest periods will be more sporadic and less rich than that occurring during continuous sensory stimulation (as during the perceptual task), thus providing superior conditions for hippocampal replay and improving memory.

The finding of a *rest*-related improvement in cognitive map accuracy is important since previous research in the field has focused on *sleep*, demonstrating, amongst others, a beneficial effect of *sleep* on the consolidation of novel spatial information (Ferrara et al., 2008; Wamsley et al., 2010) and cognitive map formation (Coutanche et al., 2013). Indeed, it has been suggested that wake and sleep consolidation have independent roles, whereby wake consolidation strengthens individual, salient memories, and sleep links and integrates related memories (Oudiette et al., 2013). Our findings suggest that the integration of information does not occur strictly during sleep, at least not in the case of spatial memory.

Research suggests that the time taken to respond in memory tests is indicative of the confidence of memory retrieval and the accessibility of a memory trace (Gimbel and Brewer,

2011). In the current study, no difference between delay conditions was observed in (i) the time taken to initiate a response and (ii) the total time taken to respond. This finding tentatively suggests that recently encoded spatial memories pertaining to the experienced environment were equally accessible in both groups, i.e. our rest delay did not enhance the retrieval of new spatial memories, but promoted the consolidation-related integration of these memories. This enhanced integration should have led to improved coding of inter-landmark relationships, a prediction that is reflected in the enhanced pointing accuracy of our wakeful rest group.

One limitation of our study is that navigation was performed in a virtual environment. However, despite the absence of body-based cues, numerous studies have shown that virtual navigation draws on similar cognitive functions as real-world navigation and recruits similar neural networks (Ekstrom et al., 2003; Wolbers and Büchel, 2005; Cushman et al., 2008). In addition, the replay of hippocampal place cells in rodents has also been observed when rodents navigate in virtual environments (Harvey et al., 2009; Dombeck et al., 2010).

In conclusion, our findings suggest that rest periods can improve spatial memory by promoting memory consolidation and integration. This could have implications for people with spatial memory problems, including patients with amnestic Mild Cognitive Impairment/Alzheimer's Disease, who often get lost, and who have been shown to benefit substantially from rest in verbal memory tests (Della Sala et al., 2005; Dewar et al., 2009, 2012b; Alber et al., 2014).

REFERENCES

Alber J, Della Sala S, Dewar M. 2014. Minimising interference with early consolidation boosts 7-day retention in amnesic patients. Neuropsychology 28:667–675.

Carr MF, Jadhav SP, Frank LM. 2011. Hippocampal replay in the awake state: a potential substrate for memory consolidation and retrieval. Nat Neurosci 14:147–153.

Coutanche MN, Gianessi CA, Chanales AJH, Willison KW, Thompson-Schill SL. 2013. The role of sleep in forming a memory representation of a two-dimensional space. Hippocampus 23:1189–97.

Craig M, Dewar M, Della Sala S, Wolbers T. 2015. Rest Boosts the Long-term Retention of Spatial Associative and Temporal Order Information. Hippocampus.

Craig M, Della Sala S, Dewar M. 2014. Autobiographical thinking interferes with episodic memory consolidation. PLoS One 9:e93915.

Csicsvari J, Dupret D. 2014. Sharp wave/ripple network oscillations and learning-associated hippocampal maps. Philos Trans R Soc Lond B Biol Sci 369:20120528.

Cushman LA, Stein K, Duffy CJ. 2008. Detecting navigational deficits in cognitive aging and
    Alzheimer disease using virtual reality. Neurology 71:888–95.

Davidson TJ, Kloosterman F, Wilson MA. 2009. Hippocampal replay of extended
    experience. Neuron 63:497–507.

Derdikman D, Moser M-B. 2010. A dual role for hippocampal replay. Neuron 65:582–584.

Deuker L, Olligs J, Fell J, Kranz TA, Mormann F, Montag C, Reuter M, Elger CE, Axmacher
    N. 2013. Memory consolidation by replay of stimulus-specific neural activity. J
    Neurosci 33:19373–19383.

Dewar M, Alber J, Butler C, Cowan N, Della Sala S. 2012a. Brief wakeful resting boosts new
    memories over the long term. Psychol Sci 23:955–960.

Dewar M, Alber J, Cowan N, Della Sala S. 2014. Boosting Long-Term Memory via Wakeful
    Rest: Intentional Rehearsal Is Not Necessary, Consolidation Is Sufficient. PLoS One
    9:e109542.

Dewar M, Cowan N, Della Sala S. 2007. Forgetting due to retroactive interference: a fusion
    of Müller and Pilzecker's (1900) early insights into everyday forgetting and recent
    research on anterograde amnesia. Cortex 43:616–634.

Dewar M, Garcia YF, Cowan N, Della Sala S. 2009. Delaying interference enhances memory
    consolidation in amnesic patients. Neuropsychology 23:627–634.

Dewar M, Pesallaccia M, Cowan N, Provinciali L, Della Sala S. 2012b. Insights into spared
    memory capacity in amnestic MCI and Alzheimer's Disease via minimal interference.
    Brain Cogn 78:189–199.

Dombeck DA, Harvey CD, Tian L, Looger LL, Tank DW. 2010. Functional imaging of

   hippocampal place cells at cellular resolution during virtual navigation. Nat Neurosci

   13:1433–1440.

Ekstrom AD, Kahana MJ, Caplan JB, Fields TA, Isham EA, Newman, Ehren L, Fried I, Dale

   J, Kandil F, Nishida S. 2003. Cellular networks underlying human spatial navigation.

   Lett to Nat 425:184–187.

Ferrara M, Iaria G, Tempesta D, Curcio G, Moroni F, Marzano C, De Gennaro L, Pacitti C.

   2008. Sleep to find your way: the role of sleep in the consolidation of memory for

   navigation in humans. Hippocampus 18:844–851.

Foster DJ, Wilson MA. 2006. Reverse replay of behavioural sequences in hippocampal place

   cells during the awake state. Nature 440:680–683.

Ghaem O, Mellet E, Crivello F, Tzourio N, Mazoyer B, Berthoz a, Denis M. 1997. Mental

   navigation along memorized routes activates the hippocampus, precuneus, and insula.

   Neuroreport 8:739–44.

Gimbel SI, Brewer JB. 2011. Reaction time, memory strength, and fMRI activity during

   memory retrieval: Hippocampus and default network are differentially responsive during

   recollection and familiarity judgments. Cogn Neurosci 2:19–26.

Gupta AS, van der Meer MAA, Touretzky DS, Redish a D. 2010. Hippocampal replay is not

   a simple function of experience. Neuron 65:695–705.

Harris M, Wolbers T. 2014. How age-related strategy switching deficits affect wayfinding in

   complex environments. Neurobiol Aging 35:1095–102.

Harvey CD, Collman F, Dombeck DA, Tank DW. 2009. Intracellular dynamics of hippocampal place cells during virtual navigation. Nature 461:941–946.

Hegarty M, Richardson AE, Montello DR, Lovelace K, Subbiah I. 2002. Development of a self-report measure of environmental spatial ability. Intelligence 30:425–447.

Ishikawa T, Montello DR. 2006. Spatial knowledge acquisition from direct experience in the environment: Individual differences in the development of metric knowledge and the integration of separately learned places. Cogn Psychol 52:93–129.

Jackson JC, Johnson A, Redish AD. 2006. Hippocampal sharp waves and reactivation during awake states depend on repeated sequential experience. J Neurosci 26:12415–12426.

Jeffreys H. 1961. Theory of probability. 3rd ed. Oxford: Oxford University Press, Clarendon Press.

Karlsson MP, Frank LM. 2009. Awake replay of remote experiences in the hippocampus. Nat Neurosci 12:913–918.

Love J, Selker R, Marsman M, Jamil T, Verhagen AJ, Ly A, Gronau QF, Smira M, Epskamp S, Matzke D, Wild A, Rouder JN, Morey RD, Wagenmakers E-J. 2015. JASP.

Mednick SC, Cai DJ, Shuman T, Anagnostaras S, Wixted JT. 2011. An opportunistic theory of cellular and systems consolidation. Trends Neurosci 34:504–514.

Moffat SD, Zonderman AB, Resnick SM. 2001. Age differences in spatial memory in a virtual environment navigation task. Neurobiol Aging 22:787–796.

Montello DR. 1998. A new framework for understanding the acquisition of spatial knowledge in large-scale environments. In: Egenhoger MJ, Golledge RG, editors. Spatial and

temporal reasoning in geographic information systems. New York: Oxford University Press. p 143–154.

Moser E, Kropff E, Moser M. 2008. Place cells, grid cells, and the brain's spatial representation system. Annu Rev Neurosci 31:69–89.

O'Keefe J, Burgess N, Donnett JG, Jeffery KJ, Maguire EA. 1998. Place cells, navigational accuracy, and the human hippocampus. Philos Trans R Soc Lond B Biol Sci 353:1333–40.

Oudiette D, Antony JW, Creery JD, Paller KA. 2013. The role of memory reactivation during wakefulness and sleep in determining which memories endure. J Neurosci 33:6672–8.

Rouder JN, Speckman PL, Sun D, Morey RD, Iverson G. 2009. Bayesian t tests for accepting and rejecting the null hypothesis. Psychon Bull Rev 16:225–237.

Della Sala S, Cowan N, Beschin N, Perini M. 2005. Just lying there, remembering: Improving recall of prose in amnesic patients with mild cognitive impairment by minimising interference. Memory 13:435–440.

Tambini A, Ketz N, Davachi L. 2010. Enhanced brain correlations during rest are related to memory for recent experiences. Neuron 65:280–290.

Tolman EC. 1948. Cognitive maps in rats and men. Psychol Rev 55:189–208.

Waller D, Beall AC, Loomis JM. 2004. Using virtual environments to assess directional knowledge. J Environ Psychol 24:105–116.

Wamsley EJ, Tucker MA, Payne JD, Stickgold R. 2010. A brief nap is beneficial for human route-learning: The role of navigation experience and EEG spectral power. Learn Mem 17:332–336.

Weisberg SM, Schinazi VR, Newcombe NS, Shipley TF, Epstein RA. 2014. Variations in cognitive maps: understanding individual differences in navigation. J Exp Psychol Learn Mem Cogn 40:669–82.

Wills T, Cacucci F, Burgess N, O'Keefe J. 2010. Development of the Hippocampal Cognitive Map in Pre-weanling Rats. Science (80-) 328:1573–1576.

Wolbers T, Büchel C. 2005. Dissociable retrosplenial and hippocampal contributions to successful formation of survey representations. J Neurosci 25:3333–3340.

Wolbers T, Hegarty M. 2010. What determines our navigational abilities? Trends Cogn Sci 14:138–46.

Wolbers T, Weiller C, Büchel C. 2004. Neural foundations of emerging route knowledge in complex spatial environments. Brain Res Cogn Brain Res 21:401–11.

FIGURE LEGENDS
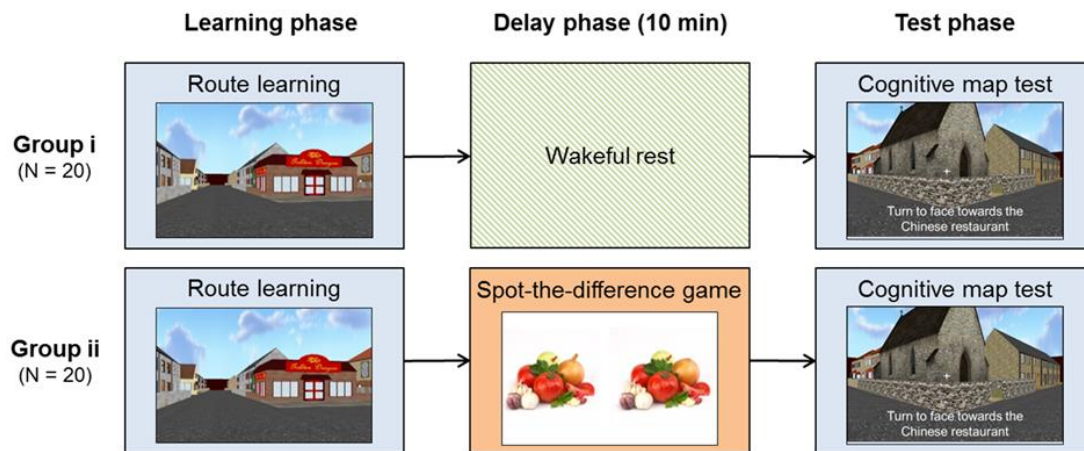
Figure 1. Procedure overview. Participants learned a novel route to criterion. Learning was followed by one of two 10-minute delay conditions: (i) wakeful rest, or (ii) an unrelated perceptual task (a spot-the-difference game). Following the delay phase, participants in both groups performed an unexpected cognitive map test comprising 16 trials.
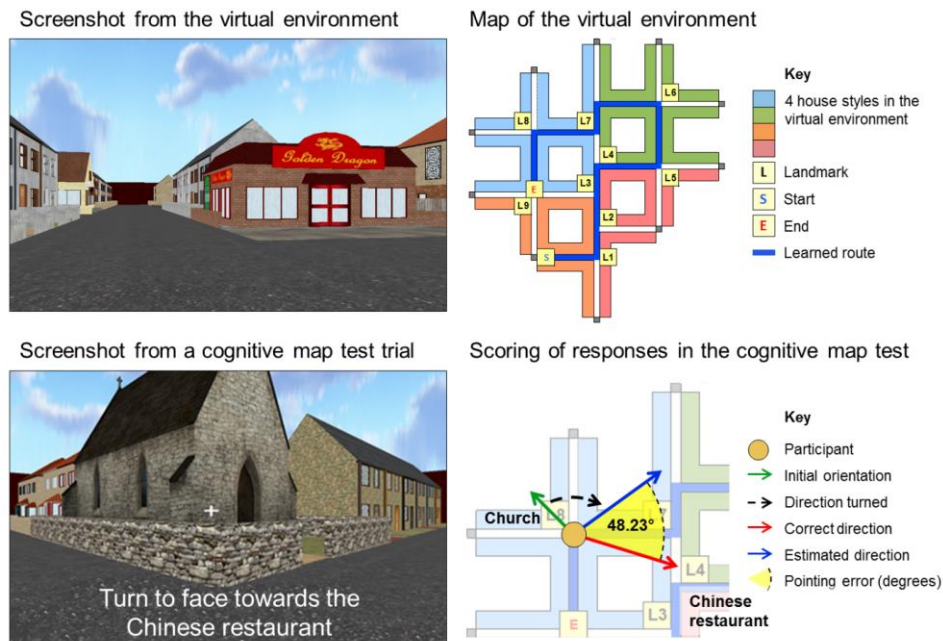
Figure 2. The virtual environment and cognitive map test. *Top left:* A screenshot of the virtual environment and an example of a landmark at a decision point (L4 - Chinese restaurant). Environment modified from Harris & Wolbers (2014). *Top right:* Map of the virtual environment. The route learned by participants is shown via the blue line; 'S' = start of route, 'E' = end of route. Landmarks (L) were all common real-world buildings: L1 = petrol station, L2 = bank, L3 = convenience store, L4 = Chinese restaurant, L5 = hotel, L6 = pet store, L7 = bar, L8 = church, L9 = hardware store. *Bottom left:* A screenshot of one of the 16 trials of the cognitive map test. *Bottom right:* An illustration of how the pointing error measure was calculated. The illustration reflects the trial shown in the image on the bottom left where the participant's initial orientation (green arrow) was directly facing the church (L8). The participant was asked to turn (black dashed arrow) to face towards the Chinese restaurant (L4). The target landmark (e.g. the Chinese restaurant) was never visible from any orientation during the cognitive map trials. The pointing error (degrees; yellow cone) between the correct direction (red arrow) and estimated direction (blue arrow) was calculated for each probe trial.
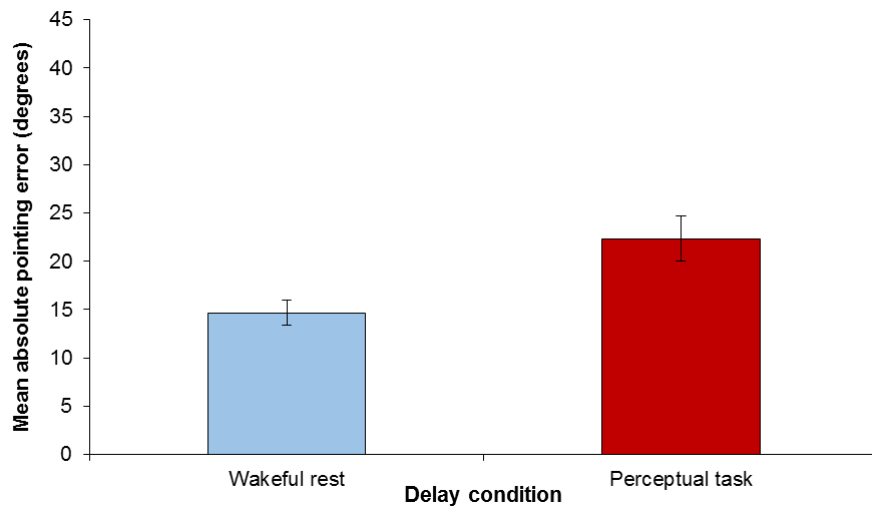
Figure 3. Performance in the cognitive map test. Mean absolute pointing error (degrees) for the wakeful rest and perceptual task groups in the cognitive map test. Error bars show the standard error of the mean.
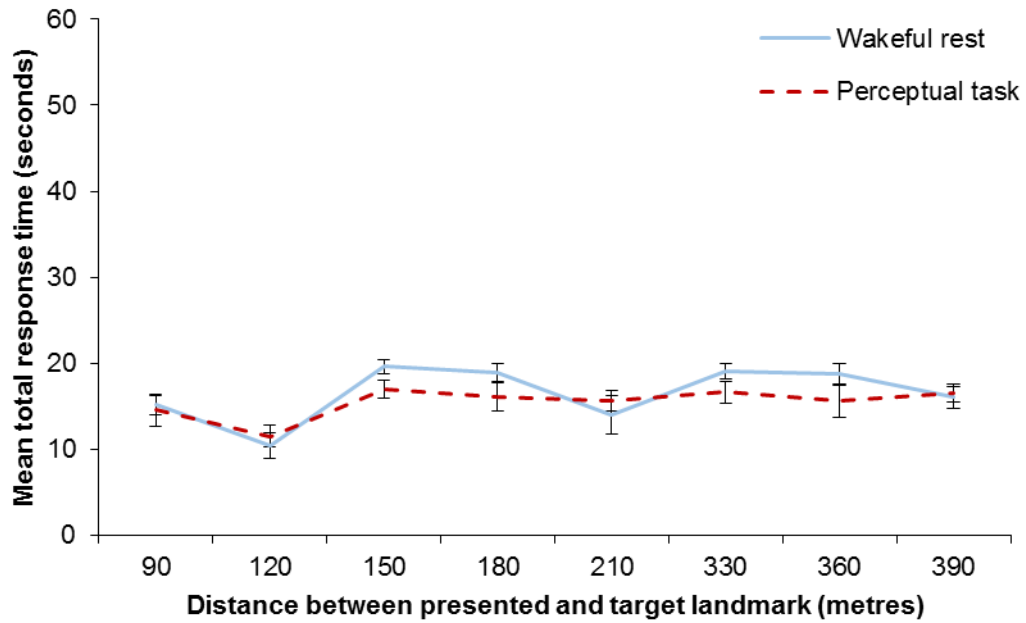
Figure 4. Cognitive map test total response times as a function of distance between presented and target landmarks. Mean total response time scores (seconds) in the cognitive map test for the wakeful rest and perceptual task groups broken down by distance between the presented and target landmarks (metres).

Table 1

Learning errors. *Mean number of errors (wrong turns) made during route learning in the wakeful rest and perceptual task groups. Standard deviations are shown in parentheses.*

Delay condition	Probe trial 1	Probe trial 2	Probe trial 3	Overall
Wakeful rest	0.35 (0.81)	0.05 (0.22)	0.00 (0.00)	0.40 (0.82)
Perceptual task	0.30 (0.80)	0.00 (0.00)	-	0.30 (0.80)

Table 1. Learning errors. Mean number of errors (wrong turns) made during route learning in the wakeful rest and perceptual task groups. Standard deviations are shown in parentheses.