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Reduced past-oriented mind wandering in left compared to right medial temporal lobe epilepsy
Mind wandering refers to a shift of attention away from a task at hand to task-unrelated thoughts. Several groups have shown increased activation of the left medial temporal lobe (MTL) before and during spontaneous thoughts suggesting that the left MTL may play a crucial role in mind wandering. Due to its relevance for long-term memory, we further hypothesized that the left MTL is particularly involved in mind wandering towards the past. Accordingly, we predicted a reduced propensity to mind wander and less past-oriented mind wandering in patients with left MTL epilepsies. To this end, we experimentally investigated mind wandering in 89 inpatients undergoing diagnostic evaluation of their putative epileptic disorder. Patients performed a sustained attention to response task with embedded experience sampling probes aiming to assess occurrence, meta-awareness and temporal orientation (past/present/future) of mind wandering episodes. We did not find significant differences in the propensity to mind wander between patient subgroups. However, the left MTL epilepsy subgroup showed significantly reduced past-oriented mind wandering compared to right MTL epilepsies, as well as a trend toward diminished past-oriented mind wandering compared to idiopathic epilepsies. Possibly due to compensatory mechanisms the right MTL epilepsy subgroup showed significantly increased past-oriented mind wandering compared to extratemporal epilepsies and patients with syncopes. These behavioral findings point to a rejection of the hypothesis that the amount of time engaged in mind wandering crucially depends on the left MTL. However, our data do support the idea that the left MTL is particularly involved in mind wandering towards the past.
Abbreviations

ANOVA: Analysis of variance
ASRS: Adult self-report scale
BDI: Beck depression inventory
CNS: Central nervous system
EEG: Electroencephalogram
fMRI: Functional magnetic resonance imaging
LSD: Least square difference
MTL: Medial temporal lobe
MW: Mind wandering
SART: Sustained attention to response task
SD: Standard deviation
Introduction

Mind wandering is reported to occupy up to half of the waking time of adult individuals (Killingsworth and Gilbert, 2010). It refers to a pervasive and ubiquitous state where attention is withdrawn from the task or situation currently at hand and drifts to internal thoughts, images or feelings, often unrelated to the task or environment. Mind wandering can have both positive and negative effects (Leszczynski et al., 2017; Mooneyham and Schooler, 2013). Amongst the positive effects are enhanced creativity and better future planning (Baird et al., 2012; Oettingen and Schwörer, 2013). The negative effects range from errors in ongoing perceptual and cognitive tasks (Christoff et al., 2009; Robertson et al., 1997) to feelings of persistent worry, increased stress levels (Killingsworth and Gilbert, 2010) and a decline in mood, particularly when mind wandering is related to past events (Ruby et al., 2013; Smallwood and O’Connor, 2011).

It remains an open question, as to which brain regions are responsible for mind wandering and for controlling its content. In general, mainly activity in default mode network and executive control regions has been shown to be related to mind wandering (Christoff et al., 2009; Mason et al., 2007). More specifically, several neuroimaging studies have pointed to a role of the left medial temporal lobe (MTL) in mind wandering (for an overview, see Fox et al., 2015). In particular, an fMRI study investigating the occurrence of spontaneous thoughts in experienced meditators indicated that the left hippocampus was the region activated first when thoughts arose (Ellamil et al., 2016). Taken together, these studies suggest that activity of the left hippocampus is crucial for mind wandering.

At least two processes, i.e. the initiation and maintenance of mind wandering contribute to its propensity, as measured by experience sampling probes (Smallwood 2013). In the present study we did not aim at disentangling these processes. Due to the suggested crucial role of the left hippocampus in mind wandering, we hypothesized that subjects with left MTL pathology would spend less time engaged in mind wandering, as measured by experience sampling probes. As the MTL is fundamental for long-term memory processes (e.g. Bird and Burgess, 2008; Eichenbaum, 2000), another more obvious idea
is that the MTL is involved in mind wandering towards the past. Therefore, we further hypothesized that subjects with left MTL pathology would spend less amounts of time engaged in mind wandering towards the past.

McCormick and colleagues (2018) investigated mind wandering in six patients with bilateral hippocampal damage and twelve age- and gender- matched healthy controls. The authors reported that patients engaged in as much mind wandering as the control subjects. However, average mind wandering was numerically smaller in the patients and the hypothesis of decreased mind wandering was rejected based on a rather low p-value (two-tailed p = 0.12). Importantly, the patients’ mind wandering was more often related to the present and less to past and future, suggesting a role of the MTL in the temporal orientation of mind wandering (McCormick et al., 2018). Recently, O’Callaghan and colleagues (2019) examined mind wandering in a large group of frontotemporal and Alzheimer dementia patients, as well in a group of age-matched controls. They observed that the propensity to mind wander was associated with grey matter integrity in the left hippocampus and left parahippocampal gyrus (O’Callaghan et al., 2019). Moreover, mind wandering scores were significantly correlated with connectivity of the left MTL with other brain regions.

To our knowledge mind wandering has not yet been directly and systematically studied in patients with epilepsy. Here, we experimentally investigated mind wandering in 89 patients admitted to our ward, undergoing assessment of their putative epileptic disorder. Based on the final outcomes of diagnostic evaluation four groups of epilepsy patients (left and right MTL epilepsy, extratemporal epilepsy, idiopathic epilepsy) and two control groups (non-epileptic dissociative seizures, cardiac syncopes) were identified. Mind wandering was assessed using a variant of the sustained attention to response task (SART) with embedded intermittent experience sampling probes. These ‘thought’ probes inquired as to whether the patients’ attention was ‘focused on or off’ the continuous monitoring task, and in the latter case, patients were presented with additional probes accessing meta-awareness and the temporal orientation (past, present, future) of mind wandering episodes. We examined the hypotheses outlined above, that a) left MTL epilepsy patients spend less amounts of time mind wandering, and b) left MTL epilepsy
patients engage in less past-oriented mind wandering compared to the other patient subgroups.

Materials and Methods

Patients

In total 89 inpatients were recruited into the study. Based on clinical evaluation we grouped them into the following six diagnostic subgroups: patients with left MTL epilepsy (n=20, mean age ± s.e.m: 49.8 ± 3.7, 10 female), patients with right MTL epilepsy (n=11, age: 43.8 ± 5.7, 5 female), patients with extratemporal epilepsy (n=20, age: 41.4 ± 4.0, 10 female), patients with idiopathic epilepsies (n=11, age: 27.2 ± 3.2, 8 female), patients with dissociative non-epileptic seizures (n=12, age: 30.7 ± 4.3, 8 female) and patients with absences caused by cardiac syncopes (n=15, age: 40.5 ± 5.1, 3 female). Diagnoses were provided by experienced senior physicians at the Dept. of Epileptology based on clinical parameters (semiology; physical, neuropsychological and psychopathological examinations), as well as the results of magnetic resonance imaging, electrocardiography and electroencephalography recordings including registration of seizures and syncopes. Diagnosis was made at the conclusion of the inpatient’s stay on the ward. Patients were recruited into the study by being personally approached by an investigator, who provided detailed written information regarding the study and how their data will be utilised. All patients were informed that the study was independent of any clinical, diagnostic or treatment procedures and that their decision whether to participate would not disadvantage them in any way. The study was approved by the Ethics Committee of the Medical Faculty of the University of Bonn, and all procedures were in accordance with the Declaration of Helsinki. All participants gave written informed consent.

Self-rating scales:

Prior to performing the behavioral task to assess mind wandering, patients were asked to complete four self-rating questionnaires: a) the mind-wandering questionnaire (MWQ; Mrazek et al., 2013); b) an attention deficit/hyperactivity scale (adult self-report scale, ASRSv1.1; Adler et al., 2003), c) a depression scale (Beck depression inventory II; Beck
et al., 1996), and d) a trait-anxiety scale (state-trait anxiety inventory, STAI-Trait; Spielberger et al., 1983). Only data from correctly completed questionnaires were subjected to statistical analyses (a) n=88, b) n=75, c) n=85, d) n=82).

SART task with embedded experience sampling probes
Patients were asked to perform a variant of the sustained attention to response task (SART; Robertson et al., 1997; see figure 1). This task required patients to continuously monitor a stream of digits (0-9) presented at the center of a computer screen for 2 sec (inter-stimulus interval: 2 sec). Digits 0-2 and 4-9 were used as non-target items and patients were required to respond by pressing the space bar, as quickly and accurately as possible. The number 3 was used as a target, which required patients to withhold the button-press. Digits in the number stream were presented in a random order. Each experimental session was conducted in the patient’s room on the ward. The investigator ensured that they would not be disturbed while performing the task.

Experience sampling
During the SART task experience sampling probes were used to examine the patients’ level of mind wandering, as well as their meta-awareness and the temporal orientation of mind wandering episodes. Fifty probes (either one-fold or three-fold) were presented at intervals jittered between 25 and 35 seconds. The initial probe inquired as to whether the patient had engaged in mind wandering immediately prior to the presentation of the probe: “Where was your attention focused directly before this probe appeared?” (possible responses: “on task” or “off task”). In case the patient chose “off task”, a second subsequent probe related to meta-awareness, was displayed: “Were you aware that your attention was off-task?” (possible responses: “aware” or “unaware”). Finally, a third probe was presented inquiring: “Were your thoughts concerned with...” (possible responses: “past” or “present” or “future”). Patients responded to each probe by pressing the relevant key indicated onscreen.

Pathology and neuropsychological data
For the patients diagnosed with MTL and extratemporal epilepsy, pathology data were acquired and classified using the following categories: hippocampal sclerosis, volume...
increase, focal cortical dysplasia/ tumor, vascular lesion and other. Results from neuropsychological tests conducted during the patient’s stay on the ward were available for 42 patients (MTL left: 13; MTL right: 6; extratemporal: 12; idiopathic: 3; dissociative: 5; syncopes: 3). Neuropsychological data comprised the following domains: intelligence, attention, verbal memory, figural memory, accentuated personality, level of education, handedness. Intelligence was assessed by a German vocabulary test which provides a measure of knowledge-based crystallized intelligence (Lehrl, 1977). Attention was quantified using a subtest of the EpiTrack® test battery (Lutz and Helmstaedter, 2005). Verbal memory was assessed by the Verbaler Lern- und Merkfähigkeitstest (VLMT; Lux et al., 1999), a modified German word list learning version of the Rey Auditory Verbal Learning Test (RAVLT). To examine figural memory we used a revised version of a German design list learning task (Diagnosticum für Cerebralschädigung/DCS-R; Lamberti and Weidlich, 1999). Accentuated personality was evaluated using the German personality inventory for persons with CNS diseases (FPZ; Helmstaedter and Witt, 2012). The individual neuropsychological domains were rated on a five-tiered scale as practiced and described before (Helmstaedter and Witt, 2012; 0 = severe impairment, i.e. at least two test scores >2 standard deviations (SD) below the mean of the normative sample (always taking age into consideration); 1 = impairment, i.e. at least two test scores >1 SD below the mean of the normative sample; 2 = borderline, i.e. at least one test score >1 SD below the mean of the normative sample; 3 = unimpaired, i.e. no test scores >1 standard deviations (SD) below the mean of the normative sample; 4 = above average, at least two test scores >1 SD above the mean score of the normative sample) based on the underlying psychometric test results.

Data analyses
The following eight measures were evaluated based on the behavioral responses during the SART task: percentage of mind wandering (i.e., of “off task” responses), percentage of meta-awareness (i.e., of “aware” responses), percentages of “past”, “present” and “future” responses, percentage of correct responses to targets, percentage of correct responses to non-targets, reaction times for non-target responses. With the exception of reaction times, data for these measures were subjected to arcsine-transformation to render normal distribution (transformed value = arcsine (square root (original value))).
Statistical analyses were performed using one-way ANOVAs with the independent factor \textsc{diagnosis} (left MTL, right MTL, extratemporal, idiopathic, dissociative, syncope). In case of a significant effect for the factor \textsc{diagnosis} post-hoc comparisons between the left MTL epilepsy group and all other groups were performed based on one-sided Dunnett’s tests. For exploratory purposes, we additionally calculated Fisher’s least square difference (LSD) post-hoc tests between all pairs of groups. Moreover, Spearman’s correlation coefficients across all patients were calculated between the scores of the four self-rating scales and the percentages of mind wandering. Furthermore, neuropsychological test scores were subjected to one-way ANOVAs with the independent factor \textsc{diagnosis} (left MTL, right MTL, extratemporal, idiopathic, dissociative, syncope; alternatively: left MTL, right MTL; and: extratemporal, right MTL).

Results

To investigate whether propensity, meta-awareness and temporal orientation of mind wandering differed between patient subgroups we conducted one-way ANOVAs with \textsc{diagnosis} as independent factor. For the propensity to mind wander (see figure 2), the levels of meta-awareness (see figure 3), and the orientation towards present and future, we found no significant effects of \textsc{diagnosis} (propensity: $F_{5,83} = 0.562; \ p = 0.73$; meta-awareness: $F_{5,74} = 1.134; \ p = 0.35$; present: $F_{5,74} = 0.326; \ p = 0.90$; future: $F_{5,74} = 0.290; \ p = 0.92$). Furthermore, there were no significant effects of \textsc{diagnosis} for the percentage of correct responses to targets ($F_{5,83} = 0.742; \ p = 0.13$), the percentage of correct responses to non-targets ($F_{5,83} = 1.777; \ p = 0.59$) and for reaction times ($F_{5,83} = 0.395; \ p = 0.85$).

We observed a significant effect of \textsc{diagnosis} for the orientation of mind wandering towards the past ($F_{5,74} = 2.428; \ p = 0.043$; see figure 4). Post-hoc one-sided Dunnett’s tests revealed less past-oriented mind wandering in the left MTL epilepsy subgroup compared to right MTL epilepsies ($p = 0.025$). Apart from this difference, additional exploratory Fisher’s LSD post-hoc tests indicated a trend for decreased past-oriented mind wandering in the left MTL epilepsy group compared to idiopathic epilepsies ($p = 0.073$). Furthermore, LSD tests pointed to increased past-oriented mind wandering in the
right MTL epilepsy subgroup compared to extratemporal epilepsies (p = 0.004), patients with syncope (0.046) and dissociative epilepsies (p = 0.062), as well as increased past-oriented mind wandering in idiopathic epilepsies compared to extratemporal epilepsies (p = 0.034).

The scores of the mind wandering questionnaire (Mrazek et al. 2013) were positively correlated with the experimentally determined propensities to mind wander (Spearman’s ρ = 0.422; p < 0.001). Moreover, overall ASRS-scores were positively correlated with mind wandering propensities (ρ = 0.309; p = 0.007), as well as its subscores for attention deficit (ρ = 0.237; p = 0.041) and hyperactivity (ρ = 0.369; p = 0.001). Furthermore, we observed a trend for a positive correlation between mind wandering propensities and BDI-II depression scores (ρ = 0.182; p = 0.095), but no significant correlation with trait-anxiety (ρ = 0.09; p = 0.42).

Pathologies for MTL and extratemporal epilepsy patients exhibited no noticeable patterns, which may be relatable to the results regarding past-oriented mind wandering (see Table 1). Moreover, exploratory one-way ANOVAs for each of the seven neuropsychology scores revealed no differences across all patient subgroups (each p > 0.15). To further explore a possible relation between the observed group differences for past-oriented mind wandering and neuropsychological traits, we calculated one-way ANOVAS only, including MTL left and MTL right epilepsy, as well as extratemporal and MTL right epilepsy. There was no difference in neuropsychology scores between MTL left and MTL right epilepsy (each p > 0.15). However, we detected differences between extratemporal and MTL right epilepsy, in terms of lower intelligence (p = 0.035) and attention scores (p = 0.048), in extratemporal epilepsy. These exploratory findings should be regarded with caution, since they were not corrected for multiple comparisons. Spearman correlations between percentages of past-oriented mind wandering and neuropsychological scores across all patient subgroups were not significant (each p > 0.05).
Discussion

In the present study we examined the occurrence and temporal orientation of mind wandering in patients with left dominant MTL epilepsy compared to five other clinically evaluated diagnostic subgroups (right dominant MTL epilepsy, extratemporal epilepsy, idiopathic epilepsy, non-epileptic dissociative seizures, and cardiac syncopes). We tested the two major hypotheses that a) left MTL epilepsy patients spend less amounts of time mind wandering, and b) left MTL epilepsy patients engage in less past-oriented mind wandering. The fact that we did not find a significant difference in the propensity to mind wander between the six diagnostic groups points to a rejection of the first hypothesis. However, in line with the findings of McCormick and colleagues (2018), we did detect evidence for decreased past-oriented mind wandering in left MTL epilepsy patients, lending support to the second hypothesis. This decrease in past-oriented mind wandering was most pronounced compared to patients with right MTL epilepsies. Of note, a recent study reported that patients exhibiting left hippocampal sclerosis showed reduced functional connectivity to default mode network structures during resting state compared to controls and patients with right hippocampal sclerosis (Zanão et al., 2019). Furthermore, a recent investigation analysing grey matter architecture found that the left parahippocampus is related to off-task focus (anterior left parahippocampus) and level of visual detail (posterior left parahippocampus) of ongoing thoughts (Ho et al. 2019).

Interestingly, we found evidence for increased past-oriented mind wandering in right MTL epilepsy patients, not only compared to patients with left MTL epilepsy, but also compared to those with extratemporal epilepsies, as well as patients with syncopes and dissociative seizures. Speculatively, this phenomenon may be caused by compensatory mechanisms enhancing functions in the left MTL during the course of right MTL epilepsy. In line with this rationale, for instance, increased subsequent memory-related fMRI activations in the left hippocampus and amygdala (Powell et al., 2007) and an inflation of left hippocampal shape (Yoo et al., 2019) have been reported in right MTL epilepsy patients compared to healthy controls. These findings tentatively suggest that memory-related functions in the left MTL may surpass normal level during the course of right MTL epilepsy to compensate for the deficient right MTL. Under the assumption that memory-
related functions overlap with functions supporting mind wandering towards the past; such an increase above the normal level, speculatively, may lead to enhanced past-related mind wandering.

Aside from this interpretation, functional coupling between the right hippocampus and other default mode network regions has been found to be related to mental time travel (towards past or future) during mind wandering (Karapanagiotidis et al., 2017). Although this result represents a more direct link between activity of the right hippocampus and the temporal aspect of mind wandering, from our view, a straightforward connection to our findings is not evident.

Interestingly, right MTL epilepsy patients did not only show increased past-oriented mind wandering when compared to extratemporal epilepsy patients, but also tested higher on intelligence and attention rating scales. While mind wandering has been suggested to be linked to fluid intelligence (e.g. Goodwin et al. 2017), our intelligence measure rather quantified knowledge-based intelligence. Moreover, these findings are based on exploratory analyses and therefore have to be regarded with caution. Future investigations may focus on more thoroughly addressing the interrelation between neuropsychological measures and mind wandering in epilepsy patients.

It should be noted that we did not aim to disentangle the initiation and maintenance of mind wandering in the present study (see e.g. Vatansever et al. 2019). The left hippocampus, for instance, has been suggested to be involved in the initiation of mind wandering (Ellamil et al. 2016), while the left dorsolateral prefrontal cortex (Turnbull et al. 2019) and the fronto-parietal control network (Kam et al. 2019) may be related to the maintenance of mind wandering. In future studies examining mind wandering in epilepsy, it would be desirable to isolate both subprocesses. Moreover, it may be interesting to further disentangle mind wandering in the form of verbal thoughts and visual images (McCormick et al. 2018), in particular, with regard to the predominant roles of the left versus right MTL in verbal/semantic versus visual/non-semantic memory (e.g. Dalton et al. 2016).
Regarding the interdependency between mind wandering and mood (Fox et al., 2018; Killingsworth and Gilbert, 2010), as well as attention deficit and hyperactivity (Lanier et al., 2019), we additionally assessed these traits using self-rating scales. As expected, we found significant positive correlations between the propensity to mind wander and attention deficit, hyperactivity and depression scores in our patient sample. Possibly, therapeutic interventions aiming at a reduction of mind wandering may be able to alleviate symptoms related to these comorbidities in the future (e.g. Chaieb et al., 2019).

To conclude, our findings do not support the hypothesis that the amount of time engaged in mind wandering crucially depends on the left hippocampus. However, our data corroborate the idea of a prominent role of the left hippocampus in past-oriented mind wandering. Future investigations should further elucidate this role based on functional methods, such as fMRI in healthy subjects or intracranial EEG in presurgical epilepsy patients.

Acknowledgements
The authors would like to thank all of the patients from the Dept. of Epileptology at the University Hospital Bonn who kindly participated in the study.

Conflict of interest
The authors have no conflicts of interest to declare.

Data availability statement
All data and accompanying analyses are archived at the Department of Epileptology, University of Bonn, Germany. Data and analyses can be made available upon reasonable request.

Funding statement
This study was conducted independently of a funding body.

Author contributions
LC, RW and JF designed the study. SK and RW recruited the patients. SK and CH collected the data. SK, LC and JF analysed the data. SK, LC, RW, CH and JF wrote the manuscript.
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Figure legends and captions

Figure 1: Schematic representation of the sustained attention to response task (SART) including experience sampling probes. Patients were instructed to respond to non-target numbers within the digit-stream (0-2, 4-9), by pressing the space-bar. When the target was shown (3), they had to withhold the button-press. Intermittently experience sampling probes inquired as to whether they were engaging in mind wandering (mind wandering probe), and if so, whether they were aware that they were doing so (meta-awareness probe) and what the temporal focus of their thoughts was (temporal orientation probe). Experience sampling probes were shown every 25-35 seconds and dismissed once the patient had indicated a response.

Figure 2: Propensities to mind wander in the different diagnostic subgroups. Percentages of mind wandering (‘off task’ responses) for the six different diagnostic subgroups: left MTL epilepsy, right MTL epilepsy, extratemporal epilepsy, idiopathic epilepsy, patients with absences due to cardiac syncopes, patients with dissociative non-epileptic seizures. Small dots: individual values; large dots: mean values across subjects; error bars: standard errors of the means.

Figure 3: Meta-awareness in the different diagnostic subgroups. Percentages of meta-awareness for the six different diagnostic subgroups: left MTL epilepsy, right MTL epilepsy, extratemporal epilepsy, idiopathic epilepsy, patients with absences due to cardiac syncopes, patients with dissociative non-epileptic seizures. Small dots: individual values; large dots: mean values across subjects; error bars: standard errors of the means.

Figure 4: Temporal orientation of mind wandering in the different diagnostic subgroups. Percentages of mind wandering towards the past, present and future for the six different diagnostic subgroups: left MTL epilepsy, right MTL epilepsy, extratemporal epilepsy, idiopathic epilepsy, patients with absences due to cardiac syncopes, patients with dissociative non-epileptic seizures. Small dots: individual values; large dots: mean values across subjects; error bars: standard errors of the means.
Table legend

Table 1: Pathology classifications for MTL and extratemporal epilepsy patients. FCD: focal cortical dysplasia.
Sustained attention to response task (SART) and experience sampling procedure

Response
Stimulus
4 7 0 3 5 8 0 5 7 3 1 4
Interstimulus interval (ISI)
2 secs
Target
Probe
Experience sampling
Probes presented every 25-35 secs

Probe 1
Where was your attention focused directly before this probe appeared?
On task Press S key
Off task Press K key

Probe 2
Were you aware that your attention was off task?
Aware Press D key
Unaware Press L key

Probe 3
Were your thoughts concerned with...
Past Press J key
Present Press K key
Future Press L key

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