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RESEARCH ARTICLE

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Even a little sleepiness influences neural activation and clinical reasoning in novices

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Abstract

Background and aims: Sleepiness influences alertness and cognitive functioning and impacts many aspects of medical care, including clinical reasoning. However, dual processing theory suggests that sleepiness will impact clinical reasoning differently in different individual, depending on their level of experience with the given condition. Our aim, therefore, was to examine the association between clinical reasoning, neuroanatomical activation, and sleepiness in senior medical students.

Methods: Our methodology replicated an earlier study but with novices rather than board-certified physicians. Eighteen final-year medical students answered validated multiple-choice questions (MCQs) during an fMRI scan. Each MCQ was projected in three phases: reading, answering, and reflection (modified think aloud). Echo-planar imaging (EPI) scans gave a time series that reflected blood oxygenation level dependent (BOLD) signal in each location (voxel) within the brain. Sleep data were collected via self-report (Epworth Sleepiness Scale) and actigraphy. These data were correlated with answer accuracy using Pearson correlation.

Results: Analysis revealed an increased BOLD signal in the right dorsomedial prefrontal cortex ($P < .05$) during reflection (Phase 3) associated with increased self-reported sleepiness (ESS) immediately before scanning. Covariate analysis also revealed that increased BOLD signal in the right supramarginal gyrus ($P < .05$) when reflecting (Phase 3) was associated with increased correct answer response time. Both patterns indicate effortful analytic (System 2) reasoning.

Conclusion: Our findings that novices use System 2 thinking for clinical reasoning and even a little (perceived) sleepiness influences their clinical reasoning ability to suggest that the parameters for safe working may be different for novices (eg, junior doctors) and experienced physicians.

KEYWORDS
clinical reasoning, fMRI, medical students, sleepiness

1 | INTRODUCTION

There are numerous conceptualizations about the nature of clinical reasoning but by far most of them (if not all of them) converge on the notion that clinical reasoning plays an important role in the process of data collection, diagnosing, and treating patients.[1] A doctor's ability to provide safe, high-quality care is thus dependent upon their ability to reason.[2,3] Further, given that most medical errors are considered the result of clinical reasoning errors,[2,4] there is significant interest in identifying and managing factors that may adversely impact on clinical reasoning.

Sleepiness, or fatigue, is well-established as influencing alertness and cognitive functioning.[5–7] Many studies have identified that impairments in cognitive performance are produced by both short- and long-term sleep deprivation[8]; see also Reference 6 for a good overview of the literature. Sleepiness is also known to impact on many domains of medical care, resulting in medical errors,[9] reduced motor performance,[10,11] increased risk of sharps injuries,[12] less participation in educational activities[13] and depressed mood.[14] These factors have contributed to the growing concern that prolonged duty hours and impaired sleep adversely impact on clinical reasoning, leading to increases in medical errors. These concerns have led to restrictions on work hours for interns and residents, some of the most vulnerable personnel in healthcare, in several countries.

But how does lack of sleep impair performance? Dual-processing theory suggest that sleepiness will impact clinical reasoning differently in different individuals.[15–19] Knowledge and clinical experience,[20] and how knowledge is mobilized and used in practice,[21] are important in clinical reasoning. Clinicians with higher levels of experience with a given disease or diagnosis are therefore more likely to use System 1 thinking in clinical reasoning compared to junior colleagues with less experience with the same disease or diagnosis. System 1 thinking is often described as a low effort system, which is "intuitive" and "experiential" or "pattern recognition," which triggers a more automated mode of thinking. On the other hand, those with less experience with a given disease or diagnosis—often more junior doctors and medical students—are likely to depend more on System 2 (analytical) thinking. System 2 thinking requires more careful processing, consciously applying rules, making clinical reasoning a much slower and cognitively demanding process. Through this theoretical perspective, we can hypothesize that sleepiness may impact less on clinical reasoning in colleagues who can quickly and efficiently identify a given disease or diagnosis than it will in those who need to use more cognitive effort to reach the same diagnostic and therapeutic reasoning.

The degrading effects of sleep deprivation on cognitive performance are reflected in alterations in underlying brain physiology and function.[6,22] Brain imaging data suggests that neuronal responsivity after sleep deprivation differs depending on the nature of the task: neurons have the capacity to respond normally or regionally when the brain is presented with a non-challenging task. However, where the task is more challenging, neuronal responsivity is diminished, resulting in poorer performance compared to non-sleep deprived people.[6] Previous studies have found significant correlations between sleepiness with prefrontal and parietal cortex activation during cognitive tasks,[3,22–27] with one of these studies examining performance in "expert performers" (eg, board-certified internal medicine physicians). However, in respect to clinical reasoning, the task may be the same, but how challenging it is to an individual, and hence the nature of cortical activation, may depend on their level of experience with the given condition. Indeed, there is some evidence that this is the case.[28] observed neural activation differences in decision-making strategies/processes employed by pre-clinical medical students and expert clinicians that could be attributed to differential use of type 1 and/or type 2 decision processes.

Our aim, therefore, was to examine the association between clinical reasoning, neuroanatomical activation, and sleepiness in senior medical students (novices), and compare this to the findings of an earlier study that used a similar methodology to examine the same issue in board-certified physicians (experts). Durning et al[27] found that physicians who reported higher sleepiness scores performed worse on licensing exam questions. Our interest was senior medical students as this group must be able to demonstrate clinical reasoning abilities,[29] are about to go into practice and work under supervision, so will be expected to reason under challenging conditions, such as when sleep deprived.

Drawing on the methodology and findings of Durning et al,[27] we hypothesized that the prefrontal and parietal cortices would show changes with our actigraphy-measured sleep variables, but the precise patterns of activation may differ in a more novice group who are likely to be using System 2 thinking. Our ultimate objective in this study was to add to knowledge and understanding of how sleep deprivation influences clinical reasoning, and so provide guidance as to how to support doctors and ensure safe and effective decision making.

Our study is firmly positioned in the transdisciplinary field of educational neuroscience—understanding the mental and biological processes involved in learning and using this to enhance learning. This is an exciting and rapidly developing area of education research globally, and one which has sparked interest in healthcare professions education.[1,3]

2 | METHODS

2.1 | Participants

We aimed to recruit 20 final year (Year 5) UK medical students as participants, a relatively standard sample size for studies in this area at the time of commencing the study (But see later for further discussion).[27,30] This group was targeted as they have substantial workplace/clinical experience having rotated around a range of clinical specialties for more than one full year, as well as early years clinical experiences. Inclusion criteria were being a senior medical student in good health. Exclusion criteria were contraindications for an fMRI exam such as certain cardiac pacemakers or other active medical devices or implants, or clinical conditions that may impair data collection, study performance, and/or proper data analysis such as extreme anxiety or claustrophobia, taking calcium channel blockers. We also excluded participants who were pregnant or did not wish their GP to be notified of any unusual, clinically significant features identified during the scan.

On gaining the necessary institutional and ethical approvals, information about the study was disseminated to potential participants via whole-cohort emails from the Year Lead/Year Administrator. The same emails were also sent to various medical student societies, with the request for these to be disseminated to their members. The study was also advertised via posters around campus and e-notice boards.

2.2 | Measurements/data collection

The following data were collected to examine (a) if individual differences in brain activity during the clinical reasoning task correlate with task performance and (b) whether individual differences in brain activity correlate with mean sleep during the previous seven days or sleepiness immediately before the task.

2.2.1 | Sleepiness

Participants wore an activity monitor on their non-dominant wrist for seven consecutive 24-hour periods, to record activity levels at 30-second intervals before the clinical reasoning/fMRI session. Data from the activity monitors was extracted and the following parameters calculated: sleep onset time (the first of at least three consecutive minutes with an activity frequency count below activity threshold); sleep offset time (the final activity frequency count below activity threshold before waking in the morning); total sleep time (TST); and wear time. Participants also completed the Epworth Sleepiness Scale (ESS)[31] just prior to entering the MRI scanner. The ESS is a brief eight-item, self-administered questionnaire that measures daytime sleepiness. Each item is scored on a 0 to 3 scale with 0 would never doze to 3—a high chance of dozing. A score of 10/24 or more is considered sleepy and a score of 18/24 or more is considered very sleepy.

2.2.2 | Clinical reasoning

We used validated multiple-choice questions (MCQs) from the American College of Physicians (ACP) Medical Knowledge Self-Assessment Program for Medical Students to assess clinical reasoning. Questions from the ACP contained items appropriate for assessment of the level of knowledge expected in the final year of medical school. We also choose several difficult questions that would challenge learners as we were trying to capture clinical reasoning performance and its potential interaction with sleep deprivation. We ensured the questions were fit for purpose in the UK context via blueprinting the questions released to us to the General Medical Council's (GMC's) Outcomes for Graduates and our local curriculum map. Our task closely mirrored that used by Durning et al[27] given there is evidence that brain activity response to sleep deprivation may be task and/or task outcome specific.[6,22]

We used MCQs so participants could push buttons on a handheld control to give their answers, thus eliminating the need for speech and minimizing potential motion impairment/noise in the images.[32] We selected questions that could fit on a single screen and contain only words (no images), which were vignette-based and required deliberation on the optimal choice of diagnosis or treatment.

2.2.3 | fMRI process and data collection

We used functional magnetic resonance imaging (fMRI) to view the neuroanatomical activation changes that occur during reasoning. This allowed us to directly observe brain areas activated during clinical reasoning.

Prior to the scan, participants were trained in the think-aloud procedure[27,33] (used in a modified way, see below) the method and layout of question presentation, and the correct use of the handheld buttons corresponding to answer options.

As per Durning et al,[27] each MCQ was projected in three phases. First, the stem (question) appeared, ending with "what is the most likely diagnosis?" but not displaying answer options, for 60 seconds ("reading" phase, Phase 1). Second, participants were then given a set time (duration 7 seconds) to choose an answer option ("answering" phase, Phase 2). Third, participants viewed the stem once again while asked to reflect silently on how they arrived at the diagnosis ("how did you establish the diagnosis for this item" ("reflection" phase, Phase 3, duration 14 seconds). This silent reflection can be considered a modified think-aloud. The "reading" phase is the baseline cognitive activity, to compare with the cognitive activities of answering and reflecting to see if these cause functional changes on top of the baseline of reading. This format allowed us to examine System 1 and 2 thinking: answering vs reading contrast gets at System 1 thinking and the reflecting vs reading contrast gets at System 2 thinking. Each participant was asked to answer 32 questions. There was a short pause between questions.

2.2.4 | Image acquisition

MRI was performed on a 3 T MRI scanner (Achieva TX-series; Philips Medical Systems, Netherlands) using an echo-planar imaging (EPI) pulse sequence of 32 contiguous sagittal slices per brain volume (TR = 2000 ms, TE = 25 ms, flip angle = 70, slice thickness = 4.5 mm). In-plane resolution was 3.4 × 3.4 mm (64 × 64 voxels). During the imaging session, a high-resolution T1-weighted image was acquired for anatomical reference (three-dimensional Gradient Recalled Echo [3D GRE]; TR = 8.3 ms, TE = 3.8 ms, flip angle = 8°). This image consisted of 160 sagittal slices with a slice thickness of 1.0 mm and an in-plane resolution of 0.93 × 0.93 mm (256 × 256 voxels). The participant's EPI scans gave a time series that reflects blood oxygenation level dependent (BOLD) signal in each location (voxel) within the brain.

2.3 | Data analysis

Given our aim was to compare how our participants compared to the board-certified physicians in Durning et al.'s earlier study,[27] we took the same approach to data analysis. Data from the activity monitors and ESS scores were then correlated with answer accuracy using Pearson correlation using SPSS version 25 (SPSS Inc., Chicago, IL).

Using SPM12 software (http://www.fil.ion.ucl.ac.uk/spm), voxels recording, we identified the BOLD signal from the three phases (reading, answering, and reflecting) for each individual, to elicit task specific findings. As a first level of analysis, contrasts were assessed between the "answer" (Phase 2) and "reflection" (Phase 3) phases and significance estimates in each voxel, or pictorial unit, of the fMRI scans (entire brain) for each participant. These BOLD signals were then assessed at the group level using t-tests. Further second-level analyses assessed the correlations between the difference in BOLD signal, sleepiness (ESS and actigraphy) and MCQ performance to determine which areas of the brain may be impacted by sleepiness.

For all analyses, regions are reported as significant at a whole brain $P < .05$ cluster level. This was achieved by a simultaneous requirement for a voxel threshold of $P < .001$ plus a minimum cluster size of 49 continuous voxels. Voxel and cluster size parameters were identified using standard Monte Carlo simulations[35] with code available at https://osf.io/3wf7b/. As described by the authors, assuming a voxel type I error, this method allows estimating a probability for each cluster extent (number of contiguous voxels). In this way, the desired correction for multiple comparisons can be enforced by using as a threshold the corresponding cluster extent.

TABLE 1 Overview of sample as M ± SD

Age (min-max)	24.36 ± 2.45 (22.34-31.69) y
Participants (female/male)	18 (11/7)
Epworth Sleepiness Scale (ESS (min-max)	5.17 ± 2.64 (0-11)
Actigraphy sleep time (min-max)	454.5 ± 57.7 (327-547) min
Wear time (min-max)	8.31 ± 2.28 (3.4-14.2) d
Correct (min-max)	10.44 ± 1.65 (7-13)
Mean response time for correct answers	3.98 ± 0.86 (2.47-5.5) s
Mean response time for incorrect answers	4.04 ± 0.58 (3.02-5.05) s

2.4 | Ethics

This study was approved by the College of Life Sciences and Medicine Ethics Research Board (CERB), University of Aberdeen. Potential participants were provided with study information in advance and gave written consent before participating in the research. It was made clear that participation was voluntary and they could withdraw at any time without disadvantage.

3 | RESULTS

Eighteen medical students took part in the study and were included in the analysis. There were 11 women and 7 men, and the mean age was 24.36 ± 2.45 (22.34-31.69) years. The mean number of correct

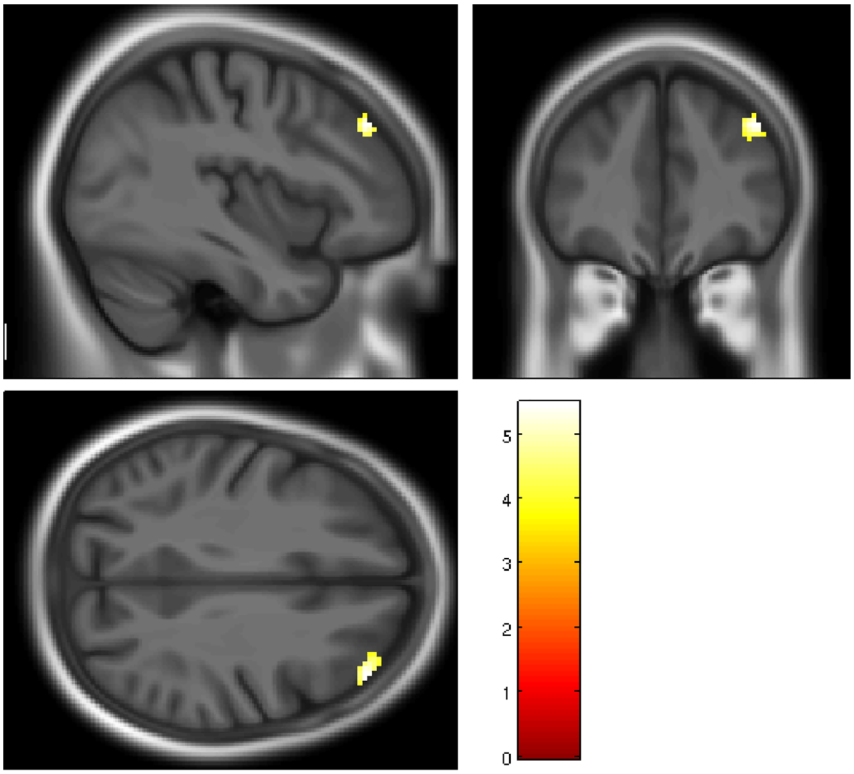

FIGURE 1 Region of significant positive correlation between Epworth Sleepiness Scale and beta values of the Reflecting > Reading contrast (color bar represents *t* score)

responses was 10.44/32 questions (range: 7-13). Epworth Sleepiness Scale (ESS) scores ranged between 0 to 11. These data plus response time to correct and incorrect MCQ answers, and mean sleep time over the preceding week are presented in Table 1.

The correlations between mean sleep time in the preceding seven days and ESS score immediately before scanning was $r(13) = 0.04$ ($P = .88$). The correlations between ESS score and MCQ score, mean sleep time and MCQ score were rho(13) = −0.28 ($P = .25$) and rho(13) = 0.005 ($P = .98$), respectively. The correlation between mean response time for correct answers and ESS score was $r(16) = 0.19$ ($P = .45$). The correlation between mean response time for correct answers and mean sleep time was $r(13) = 0.47$ ($P = .07$), while that between incorrect answers and mean sleep time was $r(13) = 0.52$ $P = .05$.

Correlation analysis revealed no significant relationship between BOLD signal during answering (answer > reading) and sleepiness. An increased BOLD signal in the right dorsomedial pre-frontal cortex (dmPFC) (FWE correction, $P < .05$) during reflection (reflecting > reading) was associated with increased self-reported sleepiness (ESS) immediately before scanning (see Figure 1 and Table 2). Correlation analysis also revealed that increased BOLD signal in the right supramarginal gyrus (FWE correction, $P < .05$) during reflection (reflecting > reading) was associated with increased correct answer response time (See Figure 2 and Table 2). Correlation analysis revealing increased BOLD signal with respect to increased self-reported sleepiness (ESS) in right pre-frontal cortex (BA 9) (top) and increased correct answer response time in the right supramarginal gyrus (BA 40) (bottom). Hemisphere (Hemi), max *t* value (*t* score) corresponding *P* values, and MNI coordinate (*X*, *Y*, *Z*) are reported in Table 2.

No other significant results were obtained.

TABLE 2 Correlation analysis

		MNI coordinates (mm)			
Region of significant correlation	***t* score**	***X***	***Y***	***Z***	***P*, FWE-corrected**
Epworth Sleepiness Scale					
Reflecting > Reading					
Right superior frontal gyrus	5.45	38	38	36	<.001
Correct answer response time					
Reflecting > Reading					
Right inferior parietal lobule	5.10	50	−38	32	<.001
Right insula	4.16	46	−32	18	<.001

Abbreviations: FWE = family-wise error; MNI = Montreal Neurological Institute.

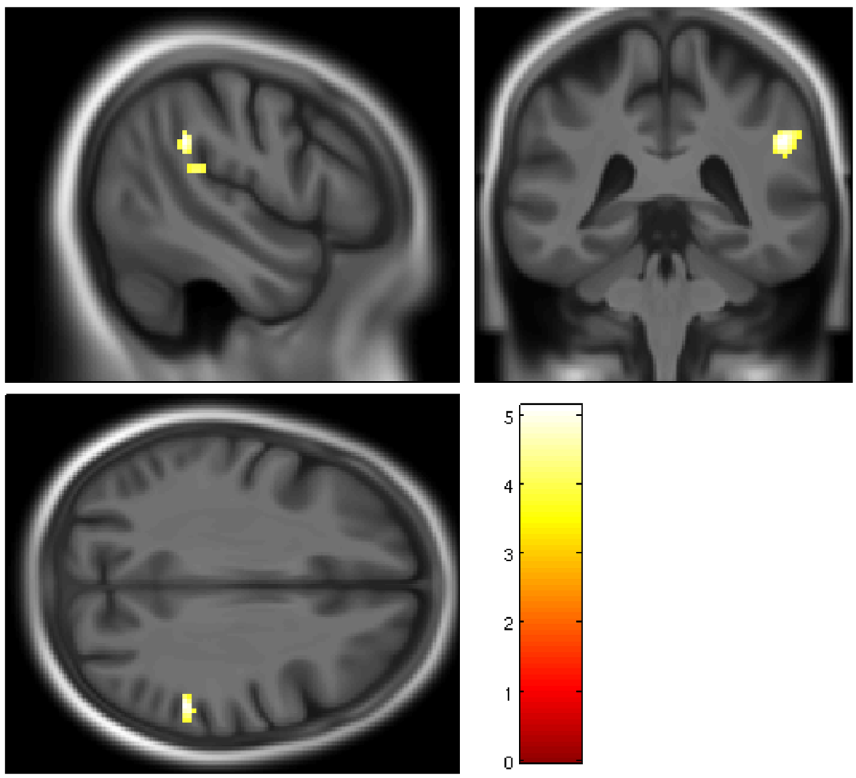

FIGURE 2 Regions of significant positive correlation between correct answer response time and beta values of the Reflecting > Reading contrast (color bar represents *t* score)

4 | DISCUSSION

4.1 | Main findings

Our aim was to examine the association between clinical reasoning, neuroanatomical activation, and sleepiness in senior medical students, and compare this to the findings of an earlier study which used a similar methodology to examine the same issue in board certified practicing physicians.[27] In doing so, we addressed an issue identified in the literature—the need for studies with a similar methodology to allow for comparisons.[34]

fMRI identified that the active areas during the clinical reasoning task were the right dorsomedial prefrontal cortex (dmPFC) and the right supramarginal gyrus, a region in the inferior parietal lobe, confirming our hypothesis in respect of areas of activation. In other words, when senior medical students and board-certified clinicians process the same task, their cortical activity is in the same regions (dmPFC and SM gyrus). However, we identified two patterns of interest. Covariate analysis revealed that increased BOLD signal in the right supramarginal gyrus during reflection (reflecting > reading) was associated with increased correct answer response time. This increased reaction time suggests participants had to think longer to get the answer while a positive correlation with Reflection suggested they then thought more about the answers they were not sure about. Both patterns indicate effortful analytic reasoning (System 2 thinking[15–18]). In short, medical students may reach the correct answer and use the same part of the brain to do so, but it takes them more effort and more cortical activity to do so than their more experienced counterparts.

We predicted that brain regions in the parietal and prefrontal lobes would show increased workload as sleepiness increased, as evidenced by increased BOLD signal. Whilst only one student in our study would be considered as sleepy in terms of self-report (ESS score), covariate analysis revealed that increased BOLD signal in the right dorsomedial prefrontal cortex (dmPFC) during reflection (reflecting > reading) was associated with increased subjective sleepiness immediately before scanning ($P < .001$). This increased BOLD signal suggests that with increasing sleepiness the participants were working harder to get the same answer (ie, engaging in System 2 processing). This relationship between sleep and reflecting is particularly interesting, suggesting that even a little (perceived) sleepiness influences clinical reasoning ability in novices. This requires further study in a larger sample.

No significant relationship was found between BOLD signal during answering (answer > reading) and subjective sleepiness suggesting that System 1 may be less affected by sleepiness. Participants had 60 seconds to read the question (Phase 1). This is quite a long time and it may be that the reading phase, rather than being merely baseline cognitive activity, was actually the phase in which hypotheses are both generated and eliminated. This merits further investigation and we propose that future studies should have four phases: reading, to be ended by the participants, showing the question, providing the answer, and showing all and asking for silent think aloud. This methodological approach can better isolate System 1/2 thinking in respect of response time.

4.2 | Comparison with previous literature

We found a weak (non-significant) correlation between a subjective judgement of daily sleepiness and an objective measurement of the amount of sleep, as per previous studies.[35–38] This supports the use of physiological measures to assess the relationship between sleepiness and clinical reasoning; self-report is unreliable,[38] and doctors may not know when they are at a level of fatigue which could be detrimental to their performance.

We did not carry out a direct comparison between medical students and their more experienced counterparts in Durning et al.'s study,[27] but rather used their findings to inform our hypothesis and adopted their methodology. Future studies should consider studying two or three groups to enable direct comparisons: perhaps senior medical students, junior doctors (eg, Foundation doctors or interns, who would likely be sleepier), and experienced clinicians.

4.3 | Strengths and weaknesses of this study

In everyday practice, clinical reasoning occurs in complex, time-pressured settings full of ill-defined problems, ambiguity,[39] and human factors associated with the environment and patient[40] as well as the clinician. In other words, clinicians must be able to make safe and effective decisions under "uncontrolled" conditions. Our study makes no claims to mimic external factors associated with the inherent uncertainty of clinical work and workplaces. We suggest however that analytical thinking will be even more effortful when sleep deprivation is coupled with time-pressure and other contextual factors. This merits further investigation, potentially via in situ studies using portable, wearable brain scanners that can monitor neural activity while a person is moving.

MCQs are one of the most common approaches for the assessment of clinical reasoning outside the workplace.[41] Our questions were drawn from the ACP, and then blueprinted against our local curriculum, so we can be confident as to their content validity and relevance. We choose questions that would challenge learners as we were trying to capture clinical reasoning performance and its potential interaction with sleep deprivation. Overall, our participants did not get many questions right. We may have pitched the level a little too high and/or our participants did not prepare for these questions in the same way they might have if they had been preparing for a formative (or indeed summative) assessment of their clinical reasoning. Future studies may wish to formally calibrate questions prior to the main study and/or use a wash-out questionnaire to gather participant perceptions of question difficulty.

The number of participants was relatively small but in keeping with recommendations for sample sizes in fMRI studies,[42] similar to previous fMRI studies in medical education,[27] and there were no other studies with medical students from which we could derive parameter estimates. However, at the time of writing up our findings new guidance was available.[43] This paper highlighted the typically small numbers in fMRI studies and proposed the need for future studies to include a sample size (power) calculation. We suspect (but do not know) that with a larger, fully powered sample some of our (non-significant) correlations would have been more impressive). Increasing sample sizes will also go some way to address challenges of reproducibility and replicability in fMRI studies.[44]

We were able to address an issue highlighted by Durning et al[27] previous pilot study of fMRI, clinical reasoning, and sleepiness by pairing the ESS, which measures self-reported sleepiness, with an objective measure of actual sleep (actigraphy).

All the measures used in the current study have been well-established in previous research and have a reasonable range of obtainable values. However, our participants were not very sleepy, and so had a limited range of scores on the ESS. We conducted our experiment during term-time when the workload in medical school is typically moderate and took care to avoid the examination period when participants might have been expected to more likely to have sleep disturbances and sleep deprivation.[45] Moreover, participants may have perceived the session as a testing situation and may have been motivated to show their best performance, compensating for any possible effect of sleepiness. Indeed, there is evidence that highly motivated participants are less prone to the effect of sleep deprivation.[46]

Our sample reflected the UK medical student population in terms of gender mix and age (most UK students enter medicine after high school [rather than as graduates]). There was little diversity in terms of participant age, and so age was not included as a variable in the analysis.

The use of fMRI for research purposes is now well-established and considered to have minimal physical and psychological risk, particularly in healthy adults.[47] Moreover, our participants were provided with written information about the study and were under no pressure to take part. No-one reported discomfort or asked for the session to be terminated early. Interestingly, informal feedback indicates that one reason for study participation was to experience what it was like to undergo an MRI exam, as this insight would help them describe the experience to patients and manage any patient anxiety once working as a doctor.

Finally, in MRI scans, subject motion is a major cause of magnetic resonance image quality degradation. Head movement was very low in our participants, as might be expected from young, healthy people.

4.4 | Implications for future research and practice

Given studies comparing cortical activity after normal sleep and sleep deprivation indicate intraindividual differences within individuals,[48] it would be worthwhile to replicate this study with medical students who report high levels of sleepiness, and/or have poor quality sleep on objective measures, or with residents with sleep deprivation (eg, after night shifts[49]). It may also be useful to systematically test the relationship between different parameters and measurements of both sleep (of which there are many[50]) and clinical reasoning (again, of which there are many—see[41] to inspire future studies on the relationship between subjective/objective sleep parameters and clinical reasoning in medical students, doctors in training and fully-trained doctors. The advent of portable magnetoencephalography (MEG) helmets opens huge, exciting possibilities for neuro-imaging research in real life clinical settings. Finally, there are associations between sleep and burnout[51,52] and sleep, burnout, and clinical reasoning,[53] so incorporating measurements of burnout into future fMRI studies might help unpack the relationship between sleep, psychological state, clinical reasoning, and cognitive processing/neural activity.

In terms of practice, our findings that novices use System 2 thinking for clinical reasoning and even a little (perceived) sleepiness influences clinical reasoning ability in novices, are important. This suggests that the parameters for safe working may be different for novices (eg, junior doctors) and experienced physicians (eg, consultants, attendings). This proposal requires further investigation with a suitably powered sample. Also, is there a way to design systems that can reduce cognitive demands in order to not exceed the capacities of novices? Failing this, is there a space for education and awareness raising—explaining to novices how they process information when tired, and the perils of depending on non-analytical reasoning if tired?[19]

Our study contributes to a growing body of knowledge about the neural mechanisms of learning.[54,55] Biological explanations of mental states that could hinder learning quality such as fatigue can inform the design and implementation of efficient instruction methods which are compatible with how the brain processes information.[55,56] We hope this small study acts as a catalyst, (re)kindling interest in an area of research that can help us understand and optimize learning in practically meaningful ways.

5 | CONCLUSION

To our knowledge, this is the first study to examine the relationship between functional neuroimaging characteristics, clinical reasoning, and sleepiness in final year medical students (relative novices in clinical reasoning). The data confirm our hypothesis that novices and experts "think differently." This increasing understanding of the neuroscientific basis of learning has implications for patient safety and systems design given that, in many healthcare systems, it is the less experienced doctors who are working long shifts and nights—the very people for whom clinical errors may be more likely when fatigued or under other stress.

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All authors have read and approved the final version of the manuscript.

JC had full access to all the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis

TRANSPARENCY STATEMENT

We confirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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