ADVANCED NEUROIMAGING: VISUALIZING TRAUMA'S IMPACT ON THE BRAIN

Educational Packet & Discussion Guide

SECTION 1: FOUNDATIONAL KNOWLEDGE

The Invisible Wounds of Trauma

Trauma's effects on the brain have historically been invisible, with symptoms often attributed to psychological processes alone rather than underlying neurobiological changes. Modern neuroimaging has revolutionized our understanding by allowing us to visualize structural, functional, and neurochemical alterations associated with traumatic experiences.

Key Principles of Neuroimaging:

- **Non-invasive visualization** of brain structure and function
- Provides **objective biomarkers** of trauma-related brain changes
- Helps bridge the gap between observable symptoms and underlying neural mechanisms
- Validates trauma survivors' experiences by demonstrating physical brain changes
- Informs more targeted treatment approaches based on specific neural patterns

Evolution of Brain Imaging:

- **Early Methods:** X-rays, pneumoencephalography (1920s-1970s)
- **First Revolution:** CT scanning (1970s)
- **Second Revolution:** MRI for structural imaging (1980s)
- **Third Revolution:** Functional imaging with fMRI, PET (1990s)
- **Current Era:** Multimodal, high-resolution imaging with advanced analysis techniques

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SECTION 2: CONVENTIONAL STRUCTURAL IMAGING

Standard clinical neuroimaging provides important but limited information about trauma's effects on the brain.

Computed Tomography (CT)

- **Technique:** Uses X-rays to create cross-sectional images of the brain
- **What It Shows:** Bone, acute bleeding, large structural abnormalities
- **Resolution:** Lower than MRI (typically 1-5mm)
- **Trauma Applications:**
  - Acute injury assessment (e.g., TBI, hemorrhage)
  - Screening for gross structural abnormalities
  - NOT sensitive to subtle trauma-related changes
- **Limitations:**
  - Radiation exposure
  - Poor soft tissue contrast
  - Cannot detect functional or microstructural changes

Standard Magnetic Resonance Imaging (MRI)

- **Technique:** Uses magnetic fields and radio waves to generate detailed anatomical images
- **Common Sequences:**
  - T1-weighted: Gray/white matter differentiation, anatomical detail
  - T2-weighted: Fluid-sensitive, detects edema and inflammation
  - FLAIR (Fluid-Attenuated Inversion Recovery): Highlights pathology by suppressing CSF signal
- **Trauma Applications:**
  - Measuring volume changes in key structures (e.g., hippocampus, amygdala)
  - Detecting visible lesions from traumatic brain injury
  - Ruling out other neurological conditions
- **Limitations for Trauma Assessment:**
  - Standard clinical MRI often appears "normal" despite significant trauma
  - Cannot detect microstructural, functional, or neurochemical alterations
  - Static images don't capture dynamic brain processes
  - Volumetric changes may be subtle and require specialized analysis

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SECTION 3: ADVANCED STRUCTURAL IMAGING

Advanced structural techniques provide insights into microstructural changes invisible to conventional imaging.

Diffusion Tensor Imaging (DTI)

- **Technique:** Measures the diffusion of water molecules in brain tissue, particularly along white matter tracts
- **What It Shows:**
  - White matter integrity and organization
  - Axonal injury and demyelination
  - Structural connectivity between brain regions
- **Key Metrics:**
  - Fractional Anisotropy (FA): Directionality of water diffusion
  - Mean Diffusivity (MD): Overall diffusion rate
  - Axial and Radial Diffusivity: Diffusion parallel and perpendicular to fiber direction
- **Trauma-Related Findings:**
  - Reduced FA in corpus callosum and fronto-limbic connections
  - Disrupted integrity of uncinate fasciculus (connecting prefrontal cortex and limbic structures)
  - Alterations in cingulum bundle (emotion regulation pathway)
  - Changes correlate with symptom severity in PTSD and trauma-related disorders

Voxel-Based Morphometry (VBM)

- **Technique:** Computational approach to analyzing structural MRI data
- **What It Shows:** Regional differences in brain tissue concentration/volume
- **Trauma-Related Findings:**
  - Gray matter volume reductions in hippocampus, amygdala, and prefrontal regions
  - Correlations between volume loss and trauma exposure/symptom severity
  - Age-dependent effects of trauma on brain development
- **Applications:**
  - Quantifying subtle volume changes across the entire brain
  - Comparing trauma survivors to healthy controls
  - Longitudinal tracking of brain changes during treatment

Cortical Thickness Analysis

- **Technique:** Measures the thickness of the cerebral cortex from structural MRI
- **What It Shows:** Millimeter-level changes in gray matter thickness
- **Trauma-Related Findings:**

    - Reduced thickness in regions involved in emotion regulation, fear processing
    - Correlations between childhood trauma and cortical thinning in adulthood
    - Potential resilience markers (preserved thickness despite trauma)

Surface-Based Morphometry

- **Technique:** Analyzes the shape, folding patterns, and surface area of the brain
- **What It Shows:** Subtle changes in cortical folding and surface features
- **Trauma-Related Findings:**
    - Altered gyrification (brain folding) patterns in trauma survivors
    - Changes in sulcal depth and cortical surface area
    - Potential developmental timing markers of trauma exposure

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SECTION 4: FUNCTIONAL NEUROIMAGING

Functional imaging reveals how trauma affects brain activity and connectivity patterns.

Functional Magnetic Resonance Imaging (fMRI)

- **Technique:** Measures blood oxygen level-dependent (BOLD) signal as an indirect marker of neural activity
- **Types:**
    - Task-based fMRI: Brain activity during specific tasks
    - Resting-state fMRI: Intrinsic connectivity during rest
- **What It Shows:**
    - Patterns of brain activation during cognitive/emotional processing
    - Functional connectivity between brain regions
    - Network-level organization and communication
- **Trauma-Related Findings:**
    - Hyperactivation of amygdala to threat stimuli
    - Reduced prefrontal cortex activation during emotion regulation
    - Altered default mode network connectivity
    - Disrupted fear extinction circuits
    - Abnormal salience network function (detecting and responding to significant stimuli)

Positron Emission Tomography (PET)

- **Technique:** Uses radioactive tracers to measure metabolic processes and neurotransmitter activity
- **What It Shows:**
  - Glucose metabolism (energy use by brain regions)
  - Neurotransmitter receptor binding and availability
  - Inflammation markers
  - Protein aggregation (e.g., tau in TBI)
- **Trauma-Related Findings:**
  - Altered metabolic activity in limbic and prefrontal regions
  - Changes in serotonin, dopamine, and opioid receptor binding
  - Neuroinflammatory patterns following trauma
  - Potential molecular signatures of PTSD and trauma-related disorders

Single Photon Emission Computed Tomography (SPECT)

- **Technique:** Similar to PET but uses different tracers and detection methods
- **What It Shows:** Regional cerebral blood flow and basic receptor binding
- **Trauma-Related Findings:**
  - Perfusion abnormalities in PTSD
  - Patterns distinguishing trauma from other psychiatric conditions
  - Potential guidance for treatment selection

Functional Near-Infrared Spectroscopy (fNIRS)

- **Technique:** Uses near-infrared light to measure oxygenated and deoxygenated hemoglobin
- **What It Shows:** Cortical activity patterns, particularly in superficial brain regions
- **Advantages:**
  - No radiation exposure
  - More tolerant of movement
  - Allows natural social interactions during scanning
- **Trauma-Related Applications:**
  - Studying parent-child interactions in traumatized dyads
  - Accessible research tool for vulnerable populations
  - Monitoring treatment response in real-world settings

SECTION 5: NEUROCHEMICAL IMAGING

These techniques provide insights into the neurochemical changes associated with trauma.

Magnetic Resonance Spectroscopy (MRS)

- **Technique:** Uses magnetic resonance to measure brain metabolites and neurotransmitters
- **What It Shows:** Concentrations of key brain chemicals, including:
  - N-acetylaspartate (NAA): Neuronal integrity marker
  - Glutamate/Glutamine: Excitatory neurotransmission
  - GABA: Inhibitory neurotransmission
  - Choline: Cell membrane turnover
  - Creatine: Energy metabolism
  - Myo-inositol: Glial marker, often related to inflammation
- **Trauma-Related Findings:**
  - Reduced NAA in hippocampus and anterior cingulate cortex
  - Altered glutamate/GABA balance suggesting excitatory/inhibitory dysregulation
  - Metabolite changes correlating with symptom severity
  - Potential biochemical markers of treatment response

PET Neurotransmitter Imaging

- **Technique:** Uses specific radioligands to bind to neurotransmitter receptors or transporters
- **What It Shows:** Density and availability of specific receptor types
- **Trauma-Related Findings:**
  - Altered serotonin transporter binding in PTSD
  - Changes in cannabinoid receptor systems
  - Dopamine system dysregulation related to reward processing abnormalities
  - Stress-induced changes in opioid receptor binding

SECTION 6: PERFUSION AND BLOOD FLOW IMAGING

These techniques visualize blood flow patterns that reflect brain activity and metabolism.

Perfusion-Weighted Imaging (PWI)

- **Technique:** MRI-based method for measuring cerebral blood flow
- **Methods:**
  - Dynamic Susceptibility Contrast (DSC): Tracks contrast agent passage
  - Arterial Spin Labeling (ASL): Magnetically labels arterial blood water

- **What It Shows:**
  - Regional cerebral blood flow (rCBF)
  - Blood volume and transit time
  - Perfusion deficits or hyperperfusion
- **Trauma-Related Findings:**
  - Altered blood flow in amygdala, hippocampus, and prefrontal regions
  - Perfusion abnormalities correlating with symptom clusters
  - Potential early marker of traumatic brain injury, even when structural imaging is normal

Arterial Spin Labeling (ASL)

- **Technique:** Non-invasive MRI method using magnetically labeled arterial blood as an endogenous tracer
- **Advantages:**
  - No contrast agent required
  - Quantitative blood flow measurements
  - Safe for repeated scanning (longitudinal studies)
- **Trauma-Related Findings:**
  - Hyperperfusion in limbic regions in acute PTSD
  - Hypoperfusion in prefrontal regions in chronic trauma-related disorders
  - Blood flow alterations that may precede structural changes

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SECTION 7: MULTIMODAL IMAGING APPROACHES

Combining multiple imaging techniques provides a more comprehensive understanding of trauma's impact.

Integration of Structural and Functional Measures

- **Approach:** Analyzing relationships between structure, function, and connectivity
- **Examples:**
  - Linking reduced hippocampal volume with memory-related functional activation
  - Correlating white matter integrity with functional connectivity strength
  - Examining how neurochemical alterations relate to activation patterns
- **Benefits:**
  - More complete understanding of brain-behavior relationships
  - Identification of compensatory mechanisms

- Better prediction of treatment response

Machine Learning and Pattern Recognition

- **Approach:** Using artificial intelligence to identify complex patterns across imaging modalities
- **Applications:**
  - Distinguishing trauma survivors from controls with greater accuracy
  - Predicting symptom development after trauma exposure
  - Identifying treatment-relevant neuroimaging biomarkers
  - Personalizing treatment approaches based on brain patterns

Longitudinal and Developmental Approaches

- **Approach:** Imaging the same individuals across time to track trauma effects
- **Applications:**
  - Distinguishing trauma consequences from pre-existing vulnerabilities
  - Tracking neural changes during and after treatment
  - Identifying sensitive periods when trauma has maximal impact
  - Studying resilience markers that predict recovery

SECTION 8: CLINICAL APPLICATIONS AND LIMITATIONS

Understanding both the potential and limitations of neuroimaging in trauma contexts.

Current Clinical Applications

- **Diagnostic Enhancement:**
  - Ruling out other conditions that may mimic trauma symptoms
  - Identifying comorbid traumatic brain injury in PTSD
  - Aiding differential diagnosis in complex presentations
- **Treatment Selection:**
  - Emerging biomarkers for medication response
  - Potential predictors of psychotherapy outcomes
  - Guiding brain stimulation approaches (e.g., TMS target selection)
- **Treatment Monitoring:**
  - Objective markers of neural change with intervention
  - Identification of residual abnormalities despite symptom improvement
  - Early indicators of response or non-response

Important Limitations

- **Technical Limitations:**
  - Spatial and temporal resolution constraints
  - Motion artifacts (particularly problematic in trauma populations)
  - Standardization challenges across centers and scanners
- **Interpretive Limitations:**
  - Group-level findings may not apply to individuals
  - Correlational nature of most observations (not causal)
  - Multiple potential interpretations of the same imaging finding
- **Practical Limitations:**
  - Cost and accessibility barriers
  - Expertise required for proper analysis and interpretation
  - Contraindications for some patients (e.g., metal implants for MRI)
- **Ethical Considerations:**
  - Potential for stigmatization or reductionism
  - Incidental findings management
  - Privacy concerns with brain data
  - Risk of overinterpreting preliminary research

Why Routine Clinical Imaging Often Appears "Normal"

- Standard clinical protocols lack sensitivity to subtle trauma-related changes
- Visual inspection misses changes detectable only with quantitative analysis
- Many trauma effects are functional or network-based rather than grossly structural
- Changes may be below conventional resolution thresholds
- Normative comparisons may be inappropriate for individual assessments

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SECTION 9: FUTURE DIRECTIONS

Emerging approaches with potential to further advance trauma neuroimaging.

Ultra-High Field Imaging

- **Development:** 7T and higher magnetic field strengths
- **Advantages:**
  - Dramatically improved spatial resolution
  - Better visualization of small structures (e.g., hippocampal subfields)
  - Enhanced neurochemical specificity in spectroscopy
- **Trauma Applications:**
  - Detailed mapping of microcircuitry disruptions

    - Layer-specific cortical analysis
    - More precise characterization of hippocampal pathology

Advanced Diffusion Techniques

- **Developments:**
    - High Angular Resolution Diffusion Imaging (HARDI)
    - Neurite Orientation Dispersion and Density Imaging (NODDI)
    - Diffusion Kurtosis Imaging (DKI)
- **Advantages:**
    - Better resolution of crossing fiber tracts
    - More specific microstructural measures
    - Distinction between different cellular compartments
- **Trauma Applications:**
    - More precise characterization of white matter pathology
    - Better detection of subtle axonal injury
    - Enhanced connectivity mapping

Real-Time fMRI Neurofeedback

- **Approach:** Providing individuals with real-time feedback on their brain activity
- **Trauma Applications:**
    - Training trauma survivors to regulate hyperactive amygdala responses
    - Enhancing prefrontal control over limbic reactivity
    - Personalizing therapeutic approaches based on individual neural patterns

Combined Brain-Body Imaging

- **Approach:** Simultaneous measurement of brain and peripheral physiology
- **Examples:**
    - Combined fMRI and autonomic monitoring
    - EEG-fMRI integration for improved temporal resolution
    - Neuroendocrine sampling with brain imaging
- **Trauma Applications:**
    - Better understanding of brain-body interactions in trauma responses
    - Characterizing stress system dysregulation more comprehensively
    - Linking central and peripheral biomarkers

SECTION 10: DISCUSSION QUESTIONS

1. How has neuroimaging changed our understanding of trauma's impact on the brain? How might this influence clinical approaches and public perception?

2. What are the advantages and disadvantages of using brain imaging findings when explaining trauma effects to survivors? How might this information be presented in a way that is empowering rather than deterministic?

3. Discuss the balance between understanding neurobiological trauma effects and avoiding reductionism. How can we honor both the biological and psychological/social dimensions of trauma?

4. How might neuroimaging findings inform trauma prevention, intervention, and treatment planning? What are the practical implications for trauma-informed care?

5. What ethical considerations should guide the use of neuroimaging in trauma populations? Consider issues of consent, incidental findings, and potential misuse of information.

6. How might neuroimaging contribute to a more nuanced understanding of resilience after trauma? What neural markers might differentiate those who develop persistent symptoms from those who recover?

7. Discuss how findings from adult neuroimaging studies might differ from studies of children or adolescents with trauma. What developmental considerations are important?

8. How might neuroimaging help bridge different theoretical models of trauma (e.g., cognitive, psychodynamic, somatic approaches)? What common ground might emerge?

SECTION 11: ACTIVITIES

Activity 1: Imaging Technique Matching Exercise

Instructions: Match each advanced imaging technique with what it primarily measures and its relevance to trauma research and clinical practice.

Techniques:

1. Diffusion Tensor Imaging (DTI)
2. Functional MRI (fMRI)
3. Magnetic Resonance Spectroscopy (MRS)
4. Positron Emission Tomography (PET)
5. Perfusion-Weighted Imaging (PWI)
6. Voxel-Based Morphometry (VBM)
7. Arterial Spin Labeling (ASL)
8. Cortical Thickness Analysis

Primary Measurements: A. Neural activity and functional connectivity B. White matter integrity and structural connectivity C. Regional gray matter volume and concentration D. Cortical gray matter thickness E. Regional cerebral blood flow (non-invasive, no contrast) F. Neurochemical and metabolite concentrations G. Molecular processes, neurotransmitter binding, metabolism H. Cerebral blood flow, volume, and perfusion parameters

Trauma Relevance: I. Reveals trauma-related disruptions in communication pathways between brain regions II. Shows hyperactivation of fear circuits and reduced regulatory control III. Identifies excitatory/inhibitory imbalances and neuronal integrity markers IV. Measures volume loss in stress-sensitive regions like hippocampus V. Detects subtle cortical changes not captured by volumetric measures VI. Maps patterns of hyperperfusion/hypoperfusion in trauma-related disorders VII. Quantifies neurotransmitter receptor changes and inflammatory markers VIII. Provides quantitative blood flow measurements correlating with symptom severity

Activity 2: Case Study Analysis

Instructions: Read the following case studies and answer the questions that follow each one.

Case Study 1: Imaging in Complex PTSD A 42-year-old woman with a history of severe childhood abuse presents with complex PTSD symptoms including emotional dysregulation, identity disturbance, relationship difficulties, and somatic complaints. Standard clinical MRI was reported as "within normal limits." As part of a research protocol, she underwent multimodal neuroimaging including DTI, resting-state fMRI, and MR spectroscopy. Results showed reduced fractional anisotropy in the uncinate fasciculus and corpus callosum, altered functional connectivity in the default mode and salience networks, and reduced N-acetylaspartate concentrations in the anterior cingulate cortex.

Questions:

1. Why might her standard clinical MRI appear normal despite these research findings?

2. How might each of the observed abnormalities relate to her clinical symptoms?
3. What treatment approaches might be informed by these neuroimaging results?
4. How would you explain these findings to the patient in an empowering way?

Case Study 2: Longitudinal Imaging in Trauma Treatment A 35-year-old combat veteran with PTSD undergoes baseline neuroimaging before starting trauma-focused psychotherapy. Initial scans show hyperactivity of the amygdala during fear processing, reduced hippocampal volume, and weakened connectivity between prefrontal regulatory regions and limbic areas. After 12 weeks of evidence-based trauma treatment and significant symptom reduction, follow-up scanning shows normalized amygdala reactivity and strengthened prefrontal-limbic connectivity, but hippocampal volume remains reduced.

Questions:

1. What do these findings suggest about different aspects of trauma recovery?
2. Why might structural changes (hippocampal volume) show different recovery patterns than functional measures?
3. How might these results inform ongoing treatment planning?
4. What hypotheses could explain the persistence of reduced hippocampal volume despite symptom improvement?

Activity 3: Neuroimaging Interpretation Challenge

Instructions: For each neuroimaging finding below, discuss:

1. What this might tell us about trauma's impact on the brain
2. Potential clinical implications
3. Limitations to consider when interpreting this finding

Findings to Interpret:

1. Reduced functional connectivity between the prefrontal cortex and amygdala during emotion regulation tasks in adults with PTSD

2. Increased activation of the dorsal anterior cingulate cortex in response to trauma reminders

3. Reduced volume of the hippocampus bilaterally in chronic PTSD, with greater reductions correlating with symptom severity

4. Altered white matter integrity in the cingulum bundle connecting the anterior cingulate cortex and limbic regions

5. Reduced GABA concentrations in the insula as measured by magnetic resonance spectroscopy

6. Increased resting cerebral blood flow in the amygdala as measured by arterial spin labeling

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SECTION 12: KNOWLEDGE CHECK

Multiple Choice Questions:

1. Which imaging technique is most appropriate for measuring white matter integrity and detecting subtle axonal injury? a) Standard structural MRI b) Functional MRI c) Diffusion Tensor Imaging d) Magnetic Resonance Spectroscopy

2. What brain structure has most consistently shown volume reductions in PTSD and trauma-related disorders? a) Cerebellum b) Primary motor cortex c) Hippocampus d) Basal ganglia

3. Which of the following is measured by functional MRI? a) Blood oxygen level-dependent (BOLD) signal b) Metabolite concentrations c) White matter tract orientation d) Neurotransmitter receptor density

4. Magnetic Resonance Spectroscopy (MRS) is particularly useful for trauma research because it: a) Provides the highest spatial resolution of any technique b) Directly measures neurotransmitter and metabolite concentrations c) Is the fastest neuroimaging technique d) Directly visualizes neural firing

5. Why might standard clinical brain imaging appear "normal" in a trauma survivor despite significant symptoms? a) Trauma never causes detectable brain changes b) The changes are functional or microstructural rather than gross structural c) Brain changes only occur in pediatric trauma d) Neuroimaging cannot detect any trauma-related abnormalities

Short Answer Questions:

1. Describe how multimodal imaging (combining different techniques) provides advantages over single-modality approaches in trauma research.

2. Explain how neuroimaging findings have contributed to our understanding of the biological basis of PTSD symptoms such as hyperarousal, intrusions, and avoidance.

3. Discuss the potential benefits and risks of using neuroimaging biomarkers to guide trauma treatment in clinical settings.

SECTION 13: SUPPLEMENTARY RESOURCES

Key Terminology:

- **BOLD Signal:** Blood Oxygen Level Dependent signal; the basis of functional MRI, reflecting changes in blood oxygenation related to neural activity
- **Connectivity:** Communication or relationships between different brain regions, either structural (physical connections) or functional (correlated activity)
- **Fractional Anisotropy (FA):** DTI measure reflecting the directionality of water diffusion, often used as a marker of white matter integrity
- **Hemodynamic Response:** Changes in blood flow, volume, and oxygenation that follow neural activity
- **Multimodal Imaging:** Combination of different imaging techniques to provide complementary information
- **Radioligand:** Radioactively labeled molecule that binds to specific receptors or proteins, used in PET imaging
- **Resting-State:** Brain activity or connectivity measured when a person is not performing any specific task
- **Voxel:** Three-dimensional pixel; the basic unit of neuroimaging data

Recommended Reading:

1. Stark EA, et al. (2015). Post-traumatic stress influences the brain even in the absence of symptoms: A systematic, quantitative meta-analysis of neuroimaging studies. Neuroscience & Biobehavioral Reviews, 56, 207-221.

2. Fenster RJ, et al. (2018). Brain circuit dysfunction in post-traumatic stress disorder: from mouse to man. Nature Reviews Neuroscience, 19(9), 535-551.

3. Duman RS, et al. (2019). Synaptic plasticity and depression: new insights from stress and rapid-acting antidepressants. Nature Medicine, 25(1), 30-36.

4. Akiki TJ, et al. (2018). Default mode network abnormalities in posttraumatic stress disorder: A novel network-restricted topology approach. NeuroImage, 176, 489-498.

5. Holmes SE, et al. (2018). Altered metabotropic glutamate receptor 5 markers in PTSD: In vivo and postmortem evidence. Proceedings of the National Academy of Sciences, 115(37), 9313-9318.

ANSWER KEY FOR ACTIVITIES

Activity 1: Imaging Technique Matching Exercise

1. DTI - B - I (White matter integrity - disruptions in communication pathways)
2. fMRI - A - II (Neural activity - hyperactivation of fear circuits)
3. MRS - F - III (Neurochemicals - excitatory/inhibitory imbalances)
4. PET - G - VII (Molecular processes - neurotransmitter changes)
5. PWI - H - VI (Cerebral blood flow parameters - hyper/hypoperfusion patterns)
6. VBM - C - IV (Regional gray matter volume - volume loss in stress-sensitive regions)
7. ASL - E - VIII (Non-invasive blood flow - quantitative measurements)
8. Cortical Thickness - D - V (Cortical gray matter thickness - subtle cortical changes)

Knowledge Check Answers

Multiple Choice:

1. c
2. c
3. a
4. b
5. b