

Learning, Memory, and Intelligence Effects

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Level of Evidence Conclusions

- **Animal Studies**

- Initial time period (>24 hours to 7 days): Moderate level of evidence
- Intermediate time period (8 days to 1 year): Moderate level of evidence
- Extended time period (>1 year): Low level of evidence

- **Human Studies**

- Initial time period (>24 hours to 7 days): Inadequate level of evidence
- Intermediate time period (8 days to 1 year): Low level of evidence
- Extended time period (>1 year): Moderate level of evidence



Animal Data

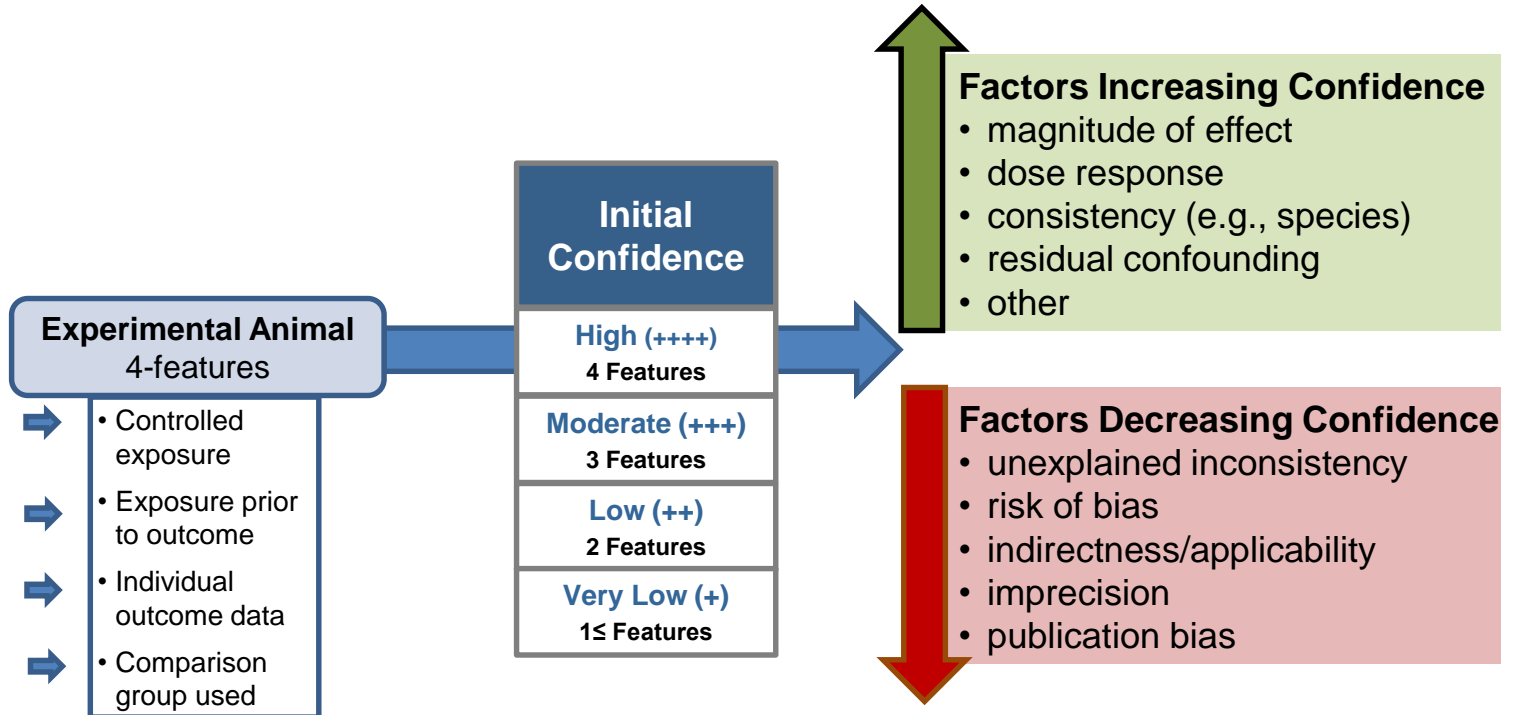
- Bodies of evidence
 - **Initial time period:** 7 studies
 - **Intermediate time period:** 7 studies
 - **Extended time period:** 2 studies
- Effects:
 - **Initial:** Effects on learning and memory
 - Evidence of impaired learning and memory in rats
 - Studies in monkeys were also available, but were limited in their ability to discern effects based on various concerns
 - **Intermediate:** Effects on learning and memory
 - Effects on learning and memory 2–6 weeks after exposure in rats
 - Studies in monkeys were also available, but were limited in their ability to discern effects based on various concerns
 - **Extended:** Inconsistencies in the two studies



Confidence Considerations to Support Level of Evidence

Animal – Learning, Memory, and Intelligence Effects

- **Initial and intermediate time periods:** 7 experimental animal studies
- **Extended time period:** 2 experimental animal studies





Confidence Considerations to Support Level of Evidence

Animal – Learning, Memory, and Intelligence Effects

- Factors that decreased confidence

All

- Risk of Bias (single study) ↓
 - Probably high for 1–3 key questions (a third with only 1)
 - Most studies probably high risk of bias for details not reported (NR) on multiple questions
 - Downgrades of 1 or 2 levels considered

Initial and Intermediate

- Imprecision ↓
 - Wide confidence intervals and large standard deviations


Extended


- Unexplained Inconsistency ↓

- Factors that increased confidence

Initial and Intermediate

- Dose Response ↑

- 
- unexplained inconsistency
 - risk of bias
 - indirectness/applicability
 - imprecision
 - publication bias

- 
- magnitude of effect
 - dose response
 - consistency (e.g., species)
 - residual confounding
 - other



Learning, Memory, and Intelligence Effects

Learning, Memory, and Intelligence Evidence Profile for Sarin										
INITIAL CONFIDENCE for each body of evidence (# of studies)	Factors decreasing confidence “---” if no concern; “↓” if serious concern to downgrade confidence					Factors increasing confidence “---” if not present; “↑” if sufficient to upgrade confidence				FINAL CONFIDENCE RATING
	Risk of Bias	Unexplained Inconsistency	Indirectness	Imprecision	Publication Bias	Large Magnitude	Dose Response	Residual Confounding	Consistency Species/Model	
<i>Animal</i>										
Initial period - Initial High (7 mammal studies)	↓	---	---	↓	---	---	↑	---	---	Moderate
Intermediate period – Initial High (7 mammal studies)	↓	---	---	↓	---	---	↑	---	---	Moderate
Extended period – Initial High (2 mammal studies)	↓	↓	---	---	---	---	---	---	---	Low

- **Moderate Confidence** that acute sarin exposure is associated with learning and memory effects in animals in the initial and intermediate time periods
- Consistent evidence of effects on learning and memory in rats through 6 weeks after exposure
- **Limitations:** risk-of-bias concerns, small sample size in some studies/groups, and heterogeneity of the data (tests used, outcomes measured, when the outcomes were measured, species tested, and method for administering sarin)



Human Data

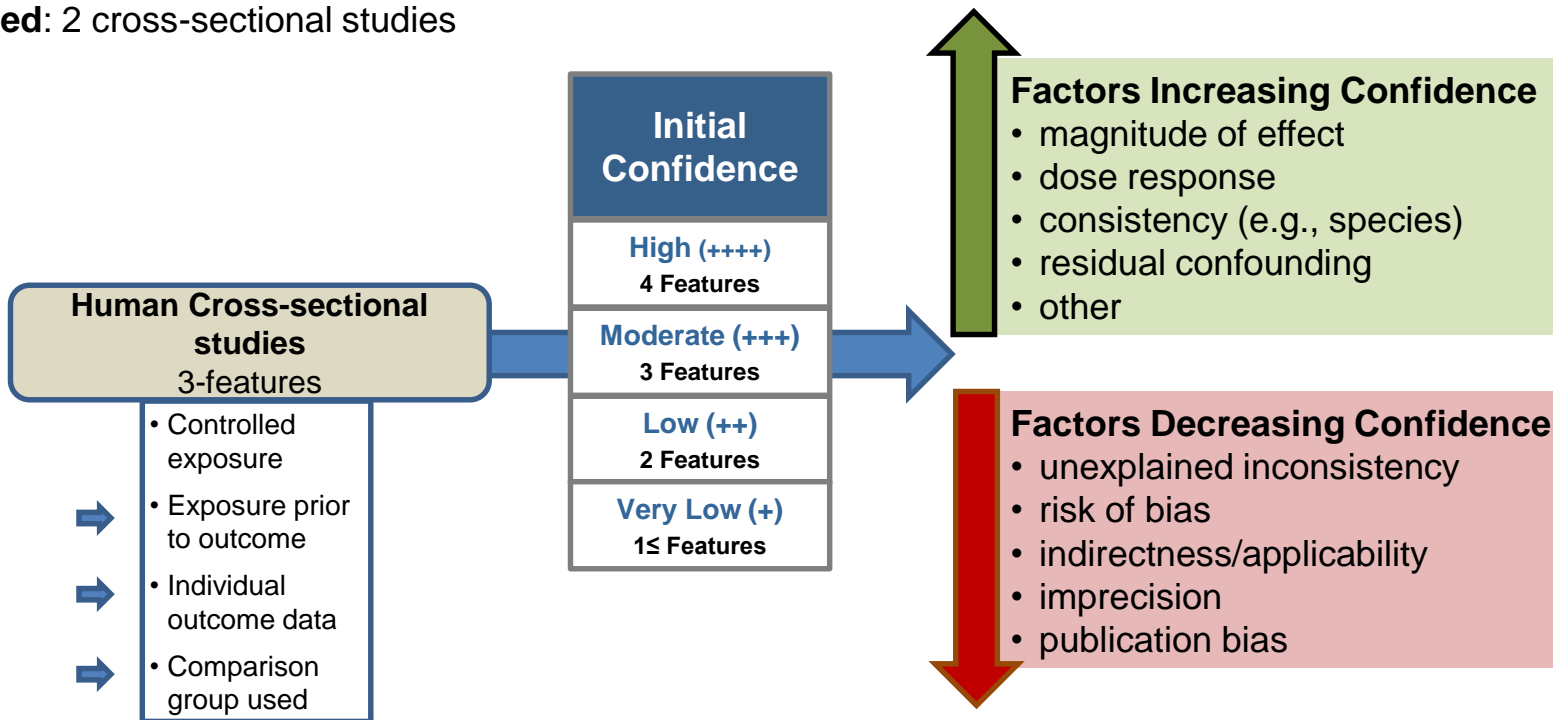
- Bodies of evidence
 - **Initial time period:** No studies
 - **Intermediate time period:** 1 cross-sectional study; 2 case reports
 - **Extended time period:** 2 cross-sectional studies; 2 case series
- Effects
 - **Intermediate:** Some evidence of impaired memory
 - Lower digit symbol test scores
 - Self-reported memory issues
 - **Extended:** Some evidence of impaired memory
 - Decreased performance on memory function tests
 - Self-reported memory issues



Confidence Considerations to Support Level of Evidence

Confidence Conclusions Primarily Based on:

- **Initial:** No studies available
- **Intermediate:** 1 cross-sectional study and 2 case reports
- **Extended:** 2 cross-sectional studies





Confidence Considerations to Support Level of Evidence

Human – Learning, Memory, and Intelligence Effects

- Factors that decreased confidence

Intermediate


- Unexplained Inconsistency ↓
 - No ability to evaluate consistency – single study


Extended

- Risk of Bias (case series) ↓
 - Probably high for 1 or 2 key questions
 - Confounding: only considered probably high in one study
 - Outcome assessment: mainly due to lack of blinding of outcome assessors

- Factors that increased confidence

- No changes for any factors for all 3 time periods

- 
- unexplained inconsistency
 - risk of bias
 - indirectness/applicability
 - imprecision
 - publication bias

- 
- magnitude of effect
 - dose response
 - consistency (e.g., species)
 - residual confounding
 - other



Learning, Memory, and Intelligence Effects

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	Risk of Bias	Unexplained Inconsistency	Indirectness	Imprecision	Publication Bias	Large Magnitude	Dose Response	Residual Confounding	Consistency Species/Model	
<i>Human</i>										
Initial period	No studies available									No rating
Intermediate period - Initial Moderate (1 cross-sectional study)	---	↓	---	---	---	---	---	---	---	Low
Intermediate period – Initial Low (2 case reports)	---	---	---	---	---	---	---	---	---	Low
Extended period – Initial Moderate (2 cross-sectional studies)	---	---	---	---	---	---	---	---	---	Moderate
Extended period – Initial Low (2 case series)	↓	---	---	---	---	---	---	---	---	Very Low

- **Moderate confidence** that acute sarin exposure is associated with effects on learning, memory, or intelligence years following acute exposure
- **Limitations:** few studies available, small number of subjects or case series with no control for comparison



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Questions?