



# International Society for CNS Clinical Trials and Methodology

**Satellite Meeting on the NIMH Initiative  
Regarding Treatment Development for  
Negative Symptoms**

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# Negative Symptom Rating Scales

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# Kraepelin's Description of Negative Symptoms

**“if we make a...survey of the psychic clinical picture of dementia praecox....we observe a weakening of those emotional activities which permanently form the mainsprings of volition....mental activity and instinct for occupation becomes mute. The result...is emotional dullness, failure of mental activities, loss of mastery over volition, of endeavor, and of ability for independent action. The essence of personality is thereby destroyed, the best and most precious part of its being, as Griesinger once expressed it, torn from her.”**

*Apathy*  
*Amotivational syndrome*

# Concepts Related to Kraepelin's Amotivational Syndrome

- **Anhedonia**
- **Type II  
schizophrenia**
- **Negative  
symptoms**

# Negative Symptoms on the Positive and Negative Syndrome Scale (PANSS)

- **Blunted Affect**
- **Emotional Withdrawal**
- **Poor Rapport**
- **Passive/Apathetic Social Withdrawal**
- **Difficulty in Abstract Thinking**
- **Lack of Spontaneity & Flow of Conversation**
- **Stereotyped Thinking (“rigid, repetitious or barren thought content”)**

# What do PANSS Negative Symptoms Reflect?

- **Blunted Affect, Emotional Withdrawal, Poor Rapport, Lack of Spontaneity & Flow of Conversation**
  - anxious, depressed, suspicious, disorganized, or unemotional and uninterested in relationships?
- **Difficulty in Abstract Thinking, Stereotyped Thinking (“rigid, repetitious or barren thought content”)**
  - absorbed in hallucinations, delusional, or cognitively impaired?

# What do SANS Negative Symptoms Reflect?

- **Impersistence at Work or School:**
  - psychotic disorganization, distracting hallucinations, or loss of interest?
- **Social Withdrawal and Social Isolation:**
  - anxious, depressed, suspicious, or unemotional and uninterested in relationships?

# Pseudospecificity

- In the context of negative symptoms and treatment trials, “pseudospecificity” refers to this problem:
  - Negative symptom rating scales can improve in a clinical trial because of improvement in other aspects of psychopathology (depression, psychotic symptoms, etc.)
- Use of path analysis and other statistical techniques to deal with this problem is controversial
- The Consensus Development Conference recommended that appropriate study designs were the best way to deal with the problem

# Negative Symptoms, Quality of Life, and Level of Function

## *SANS items:*

- Grooming and Hygiene
- Impersistence at Work or School
- Recreational Interests and Activities
- Sexual Interest and Activity
- Ability to Feel Intimacy and Closeness
- Relationships with Friends and Peers
- Social Inattentiveness
- Inattentiveness during Mental Status Testing

# Do Negative Symptom Rating Scales Quantify Kraepelin's Weakening of Volition?

- ❖ In clinical trials, negative symptoms usually improve as positive symptoms do
- ❖ Multiple causes other than “a weakening of the mainsprings of volition”
  - ❖ psychotic confusion
  - ❖ depression
  - ❖ suspicious withdrawal
  - ❖ disorganization
- ❖ Overlap with measures of level of function and quality of life

# Negative Symptoms: Concept and Reality

- **What is of interest is the clinical picture of the apathetic, unemotional, asocial patient**
- **What is measured by negative symptom scales is something broader**
- **It is either meaningless or tautological to say that negative symptoms predict quality of life and level of function, as negative symptom rating scales measure those things directly**